CHAPTER 11

Intraocular Tumours

Iris tumours

Iris melanoma

In general, uveal melanomas are three times commoner in patients with blue/grey than brown irides. They are extremely rare in black people and there is no sexual predilection. Conditions associated with or predisposed to early-onset uveal melanomas are: (a) *ocular melanocytosis*, (b) *naevus of Ota*, (c) *dysplastic cutaneous naevi*, (d) *familial melanoma* and (e) *neurofibromatosis-1*. Iris melanoma makes up about 5% of uveal melanomas. The majority are composed of spindle B cells (*see* below) and are of low malignancy. A minority contain an epithelioid cell component and can be aggressive. The tumour usually grows very slowly along the iris surface and may invade the angle and anterior ciliary body. The prognosis is very good and only about 5% of patients develop metastases.

Clinical features

1. **Presentation** is in the fifth to sixth decades, a decade earlier than ciliary body and choroidal melanoma, with enlargement of a pre-existing iris lesion.
2. **Signs**
   a. Typical
   - A pigmented or non-pigmented nodule at least 3 mm in diameter and 1 mm thickness located in the *inferior half* of the iris with a smooth or irregular surface (Fig. 11.1). Surface vascularity is also present and is easier to detect in a non-pigmented (Fig. 11.2) than a highly pigmented tumour, where it may be masked.
   - Pupillary distortion, ectropion uveae and occasionally localized cataract may be seen (Fig. 11.3).
   - Features associated with a prominent epithelioid cell component include prominent vascularity, rapid growth and heterogeneous pigmentation.



Fig. 11.2
Non-pigmented iris melanoma with prominent surface vessels

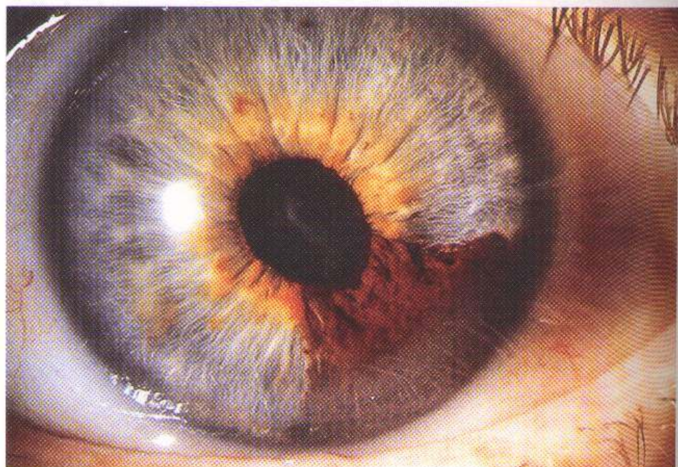


Fig. 11.3
Iris melanoma causing distortion of the pupil, ectropion uveae and a localized lens opacity

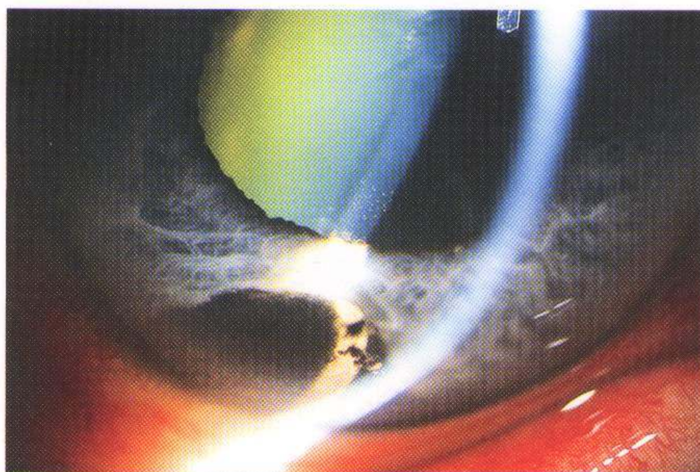


Fig. 11.1
Pigmented iris melanoma

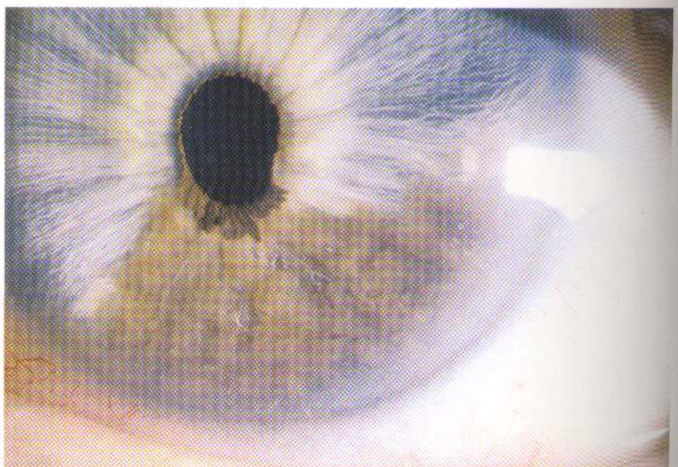


Fig. 11.4
Tapioca iris melanoma (Courtesy of B. Damato)

b. Rare variants

- Diffusely growing intrastromal melanoma may give rise to ipsilateral hyperchromic heterochromia.
- 'Tapioca melanoma' is characterized by multiple surface nodules (Fig. 11.4).

Treatment

1. **Observation** of suspicious lesions involves documentation by slit-lamp examination, gonioscopy and photography. Follow-up should be lifelong because growth may occur after several years of apparent inactivity. Initially the patient is reviewed after 3–6 months, then 6–9 months and later annually.
2. **Iridectomy** for small tumours with iris reconstruction to reduce postoperative photophobia.
3. **Iridocyclectomy** for tumours invading the angle (Fig. 11.5).
4. **Radiotherapy** with local plaques (brachytherapy) or external irradiation with charged particles for non-resectable tumours.
5. **Enucleation** may be required for diffusely growing tumours.

Differential diagnosis

1. **Iris naevus**, if large and distorting the pupil (*see* Fig. 11.11).
2. **Ciliary body melanoma** with extension through the iris root (*see* Fig. 11.24).
3. **Metastasis** to the iris is rare and usually occurs in patients with a known systemic malignancy. It is a pink or yellow, fast-growing mass (Fig. 11.6) which may be associated with anterior uveitis and occasionally hyphaema. Small, multiple deposits may also be seen (Fig 11.7).
4. **Adenoma of the iris pigment epithelium** is a rare benign tumour characterized by a dark grey-black nodule with a smooth but sometimes multinodular surface, most frequently in the peripheral iris (Fig. 11.8). The lesion causes anterior displacement and thinning of the iris stroma, which eventually erodes, disclosing the tumour on slit-lamp biomicroscopy.
5. **Leiomyoma** is an extremely rare benign tumour which arises from smooth muscle. The appearance is similar to that of an amelanotic melanoma except that it is not necessarily confined to the inferior half of the iris (Fig. 11.9). Often the diagnosis can be established only histologically.
6. **Primary iris cyst** (*see* below).



Fig. 11.5
Gonioscopic view of iris melanoma involving the angle

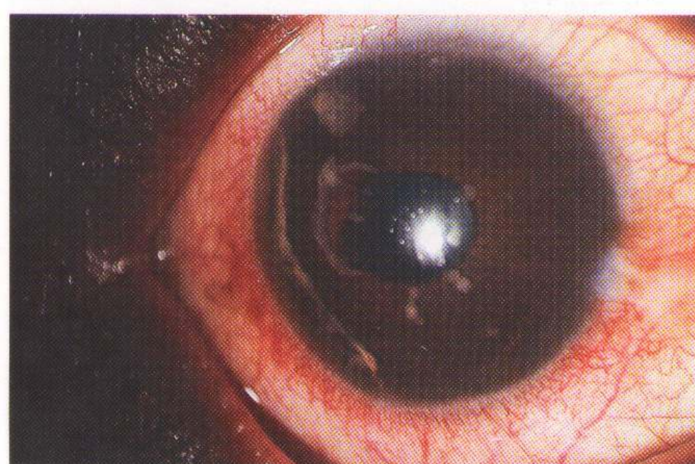


Fig. 11.7
Multiple iris metastases (Courtesy of B. Damato)

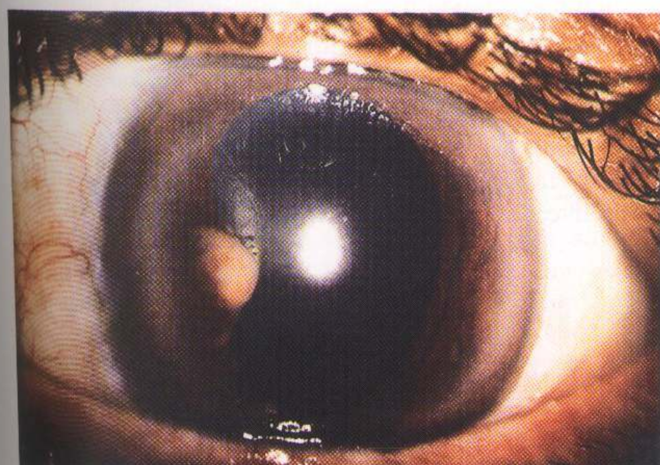


Fig. 11.6
Solitary iris metastasis

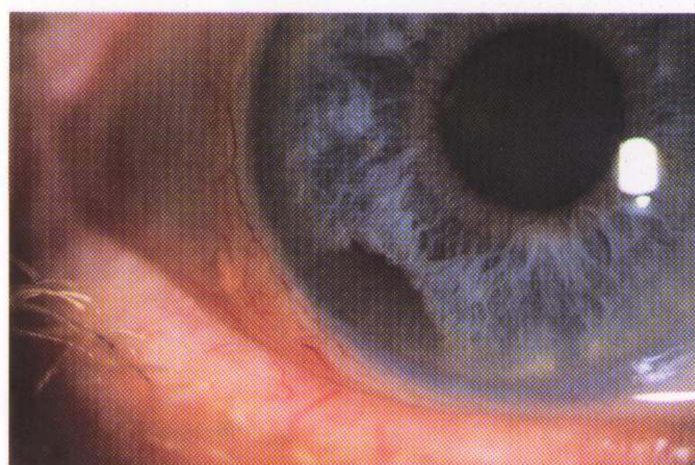
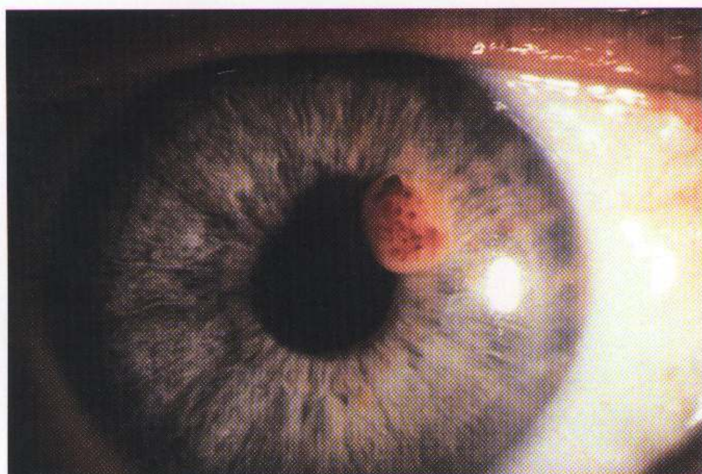
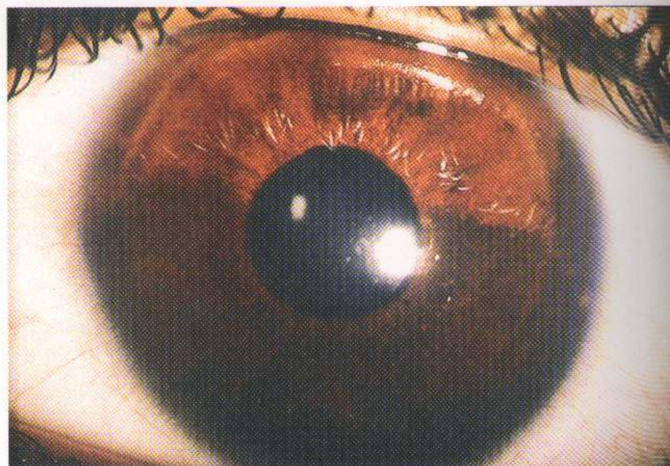
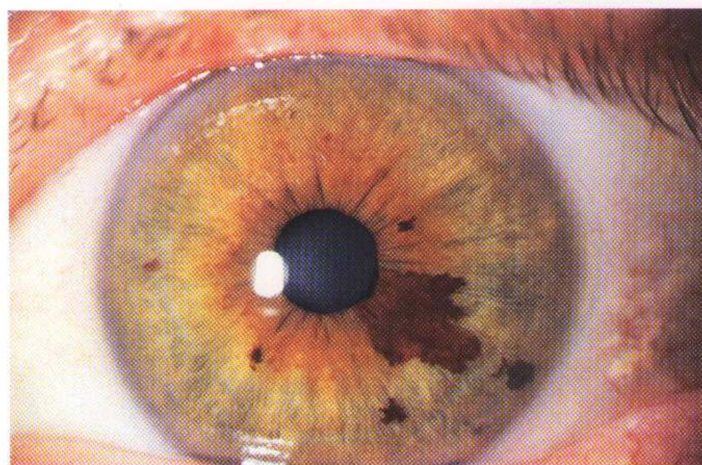


Fig. 11.8
Adenoma of the iris pigment epithelium


Fig. 11.9
Iris leiomyoma


Fig. 11.12
Diffuse iris naevus


Fig. 11.10
Iris naevus and freckles

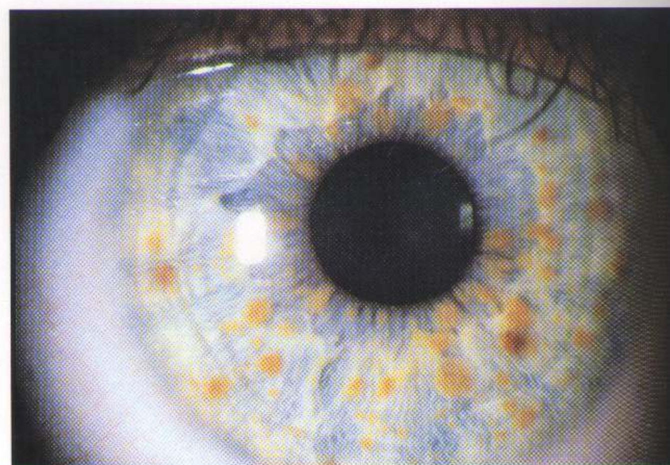

Fig. 11.13
Lisch nodules


Fig. 11.11
Iris naevus distorting the pupil

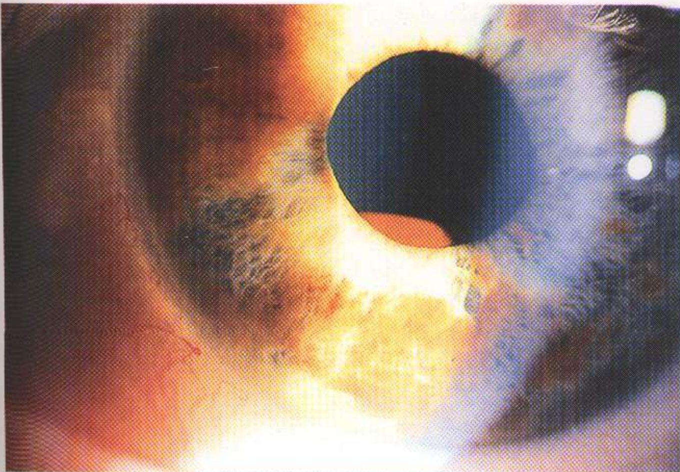
Iris naevi

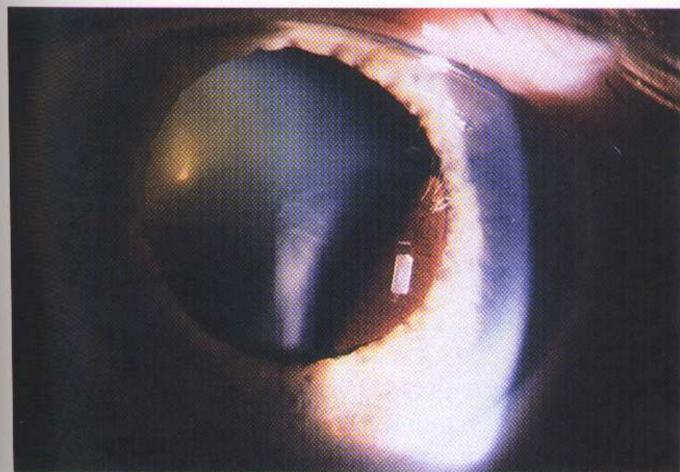
1. **A typical naevus** is a pigmented, flat or slightly elevated lesion, usually less than 3mm in diameter (Fig. 11.10). It is located in the superficial layers and may occasionally cause mild distortion of the pupil and ectropion uveae (Fig. 11.11).
2. **A diffuse naevus** obscures normal iris crypts and gives rise to hyperchromic heterochromia (Fig. 11.12). It may be seen in patients with the *Cogan–Reese syndrome* (*see* Chapter 9) and may also show small pedunculated nodules resembling mammillations.
3. **Lisch nodules** are multiple, small, bilateral, melanocytic hamartomas found after the age of 16 years in virtually all patients with neurofibromatosis-1 (Fig. 11.13).
4. **Freckles** are smaller than naevi (*see* Fig. 11.10). They are frequently multiple and bilateral, but never distort the iris architecture.

Iris cysts

Primary cysts

Primary iris cysts are rare curiosities arising from the pigment epithelium or, rarely, the stroma. The vast majority,


Fig. 11.14
Pupillary epithelial iris cyst


Fig. 11.15
Mid-zonal epithelial iris cyst

particularly those arising from the pigment epithelium, are stationary and asymptomatic.

1. **Epithelial** cysts are unilateral, solitary, dark-brown, globular structures which transilluminate. They may be located at the pupillary border (Fig. 11.14), in the mid-zone (Fig. 11.15) or the iris root. Occasionally the cysts become dislodged and float freely in the anterior chamber or vitreous. The vast majority are innocuous and rarely require treatment.
2. **Stromal** cysts present in the first year of life. They are solitary, unilateral, have a smooth, translucent anterior wall and contain fluid (Fig. 11.16). The cyst may remain dormant for many years or suddenly enlarge and cause secondary glaucoma, corneal decompensation and show a fluid–debris level reminiscent of a pseudo-hypopyon (Fig. 11.17). Occasionally the cyst may break free from the iris and float in the anterior chamber or migrate to another location. Although spontaneous regression can occur, most require treatment by needle aspiration or surgical excision.

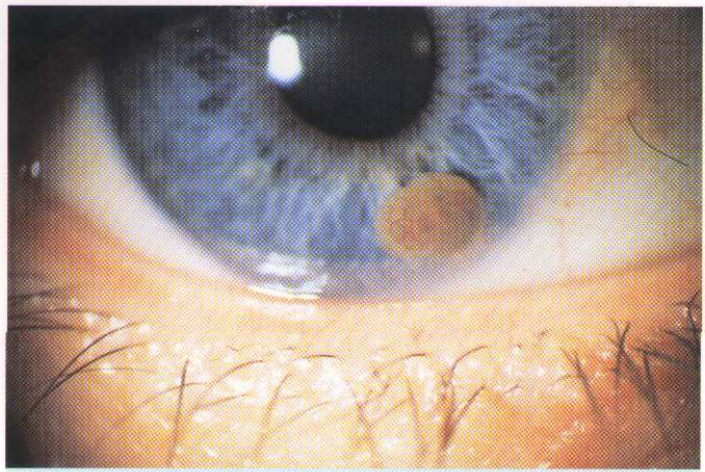
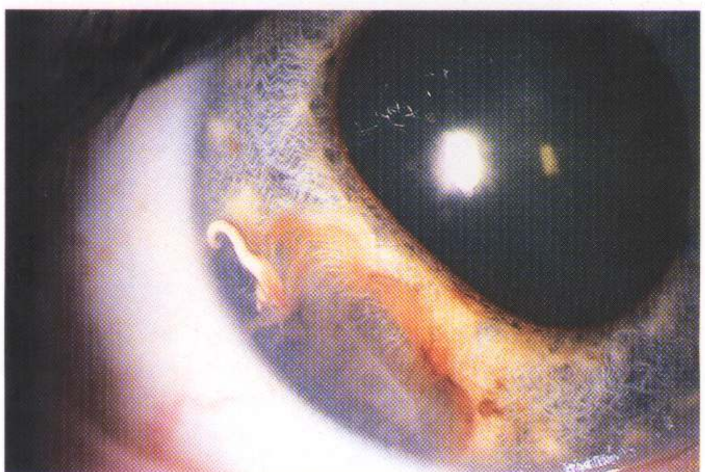
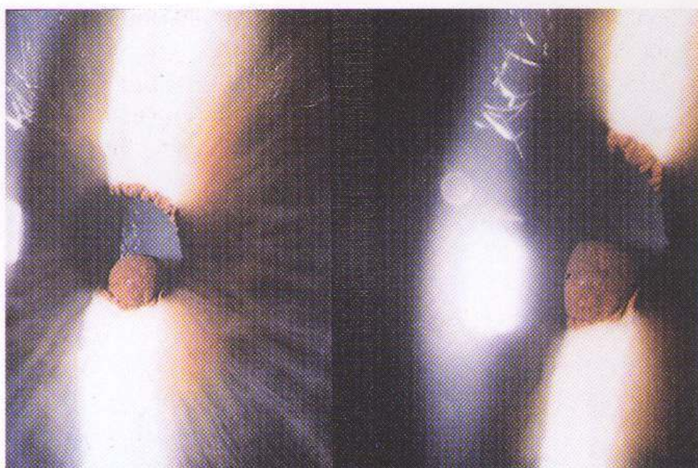

Fig. 11.16
Primary stromal iris cyst

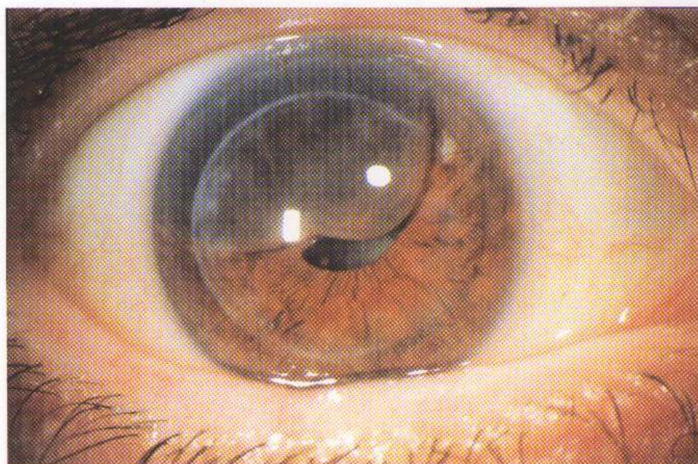

Fig. 11.17
Primary stromal iris cyst containing a fluid–debris level

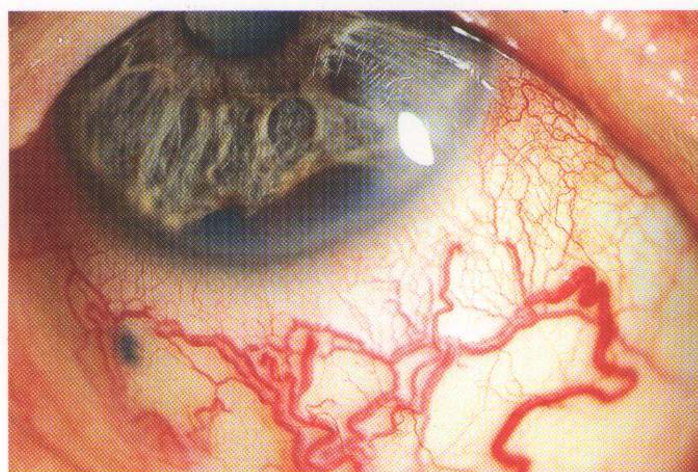

Fig. 11.18
Secondary iris cyst containing a worm

Secondary cysts

Secondary iris cysts develop as a result of implantation, parasites (Fig. 11.18), tumours or the prolonged use of


Fig. 11.19
Secondary iris cysts due to topical administration of long-acting miotics


Fig. 11.20
Secondary iris cyst following corneal grafting


Fig. 11.21
Sentinel vessels associated with ciliary body melanoma
(Courtesy of B. Damato)

long-acting miotics. The latter are usually bilateral, small, multiple and located along the pupillary border (Fig. 11.19). Their development can be prevented by the use of topical 2.5% phenylephrine. Implantation cysts originate by deposition of surface epithelial cells from the conjunctiva or cornea on the iris after penetrating or surgical trauma and may lead to the following:

1. **Pearl** cysts are small, white, solid lesions with opaque walls located in the stroma and are not connected to the wound.
2. **Serous** cysts are translucent, filled with fluid and may be connected to the wound (Fig. 11.20). They frequently enlarge, leading to corneal oedema, anterior uveitis and glaucoma. Ultrasound biomicroscopy may show the location and extent of the lesions when surgical excision is contemplated.

Ciliary body tumours

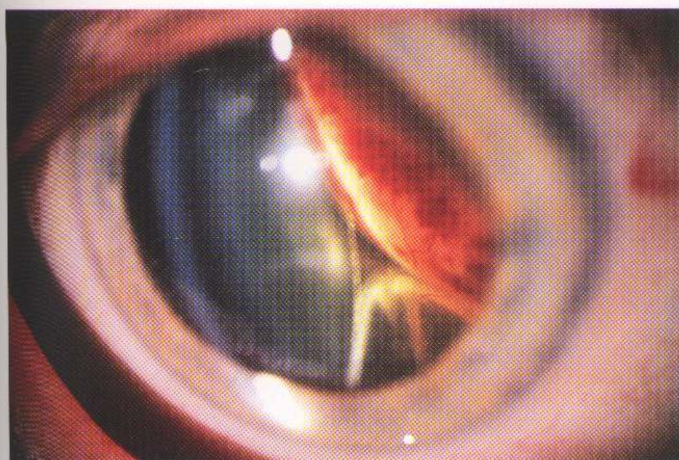
Ciliary body melanoma

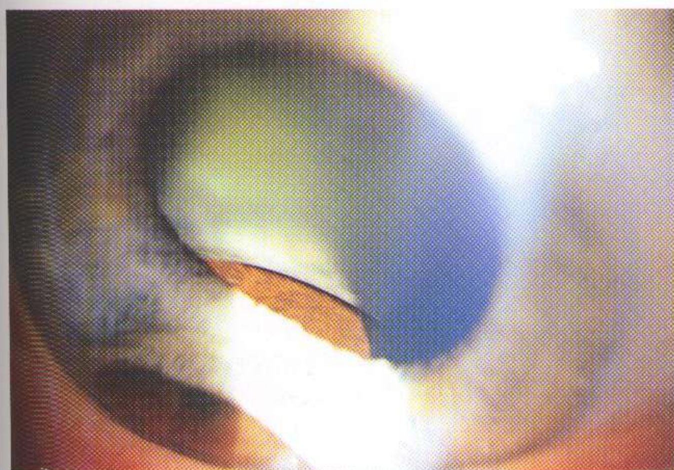
About 10% of uveal melanomas arise from the ciliary body.

Clinical features

1. **Presentation** is in the sixth decade with visual symptoms but occasionally the tumour may be discovered incidentally.
2. **Signs** depend on the size and location of the tumour. Small localized tumours cannot usually be visualized without pupillary dilatation and gonioscopy.
   - Dilated episcleral blood vessels in the same quadrant as the tumour (sentinel vessels) (Fig. 11.21).
   - Extraocular extension through the scleral emissary vessels may produce a dark epibulbar mass (Fig. 11.22) which may be mistaken for a conjunctival melanoma.
   - Pressure on the lens may give rise to astigmatism, subluxation or cataract (Fig. 11.23).
   - Erosion through the iris root may mimic iris melanoma (Fig. 11.24).
   - Retinal detachment may be caused by posterior extension.


Fig. 11.22
Extraocular extension of ciliary body melanoma


Fig. 11.23
Ciliary body melanoma displacing the lens (Courtesy of C. Barry)


Fig. 11.24
Ciliary body melanoma eroding the iris root

- Anterior uveitis, caused by tumour necrosis, is uncommon.
- Circumferential (annular) growth for 360° carries the worst prognosis because early diagnosis is difficult.

Investigations

1. **Triple-mirror contact lens** examination through a well-dilated pupil is essential and is particularly useful in detecting forward erosion through the iris root into the angle.
2. **Transillumination** may give an approximate indication of tumour extent but is of little diagnostic value because an amelanotic melanoma may transilluminate.
3. **Ultrasonic biomicroscopy** is useful in eyes with opaque media and also shows dimensions and extent.
4. **Biopsy** may be helpful in selected cases.

Treatment

1. **General considerations** (*see* choroidal melanoma below).
2. **Enucleation** for large tumours and those affecting the anterior choroid. Secondary glaucoma, resulting from extensive invasion of Schlemm canal, is also an indication for enucleation.
3. **Iridocyclectomy** for small or medium-sized tumours involving no more than one-third of the angle. Complications are vitreous haemorrhage, retinal detachment and incomplete resection.
4. **Radiotherapy** by brachytherapy or external beam irradiation in selected cases.

Differential diagnosis

1. **Uveal effusion syndrome** (*see* Fig. 12.66) may resemble circumferential ciliary body melanoma. However, the effusion is lobulated, transilluminates brightly and appears cystic on ultrasonography.
2. **Congenital epithelial iridociliary cysts** may displace the lens but can be readily differentiated from melanomas by ultrasonography.
3. **Other ciliary body tumours**, which are extremely rare, include medulloepithelioma, metastases, adenocarcinoma, cystic adenoma and leiomyoma. In most of these the correct diagnosis can be made only histologically.

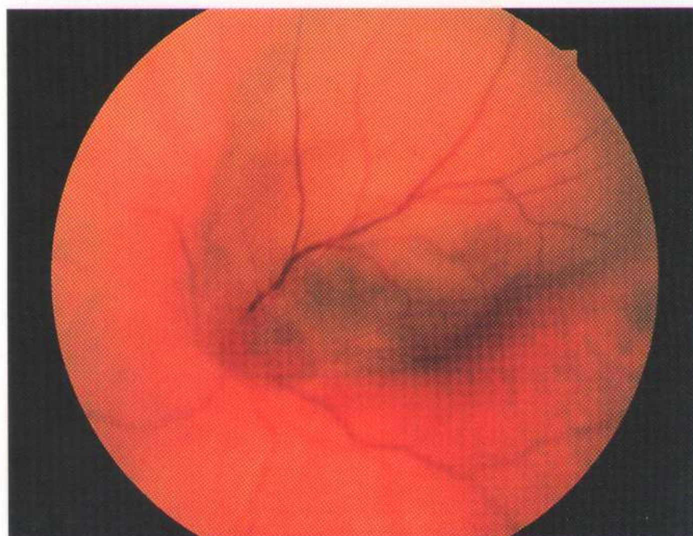
Choroidal tumours

Choroidal melanoma

Melanoma of the choroid is the most common primary intraocular tumour in adults and accounts for 85% of uveal melanomas.

Clinical features

1. **Presentation** is usually during the sixth decade (range fifth to eighth) in one of the following ways:


Fig. 11.25
Choroidal melanoma

- An asymptomatic tumour detected by chance.
- A symptomatic tumour causing decreased visual acuity or a visual field defect.
- About a third of patients complain of very brief 'balls of light' travelling across the visual field two to three times a day, most apparent in subdued lighting.

2. Signs

- An elevated, subretinal, dome-shaped, brown or grey mass (Fig. 11.25). Occasionally the tumour may be mottled with dark-brown or black pigment, or be virtually amelanotic (Fig. 11.26). Surface orange pigment (lipofuscin) is common but not diagnostic.
- If the tumour breaks through Bruch membrane it acquires a mushroom-shaped appearance (Fig. 11.27).

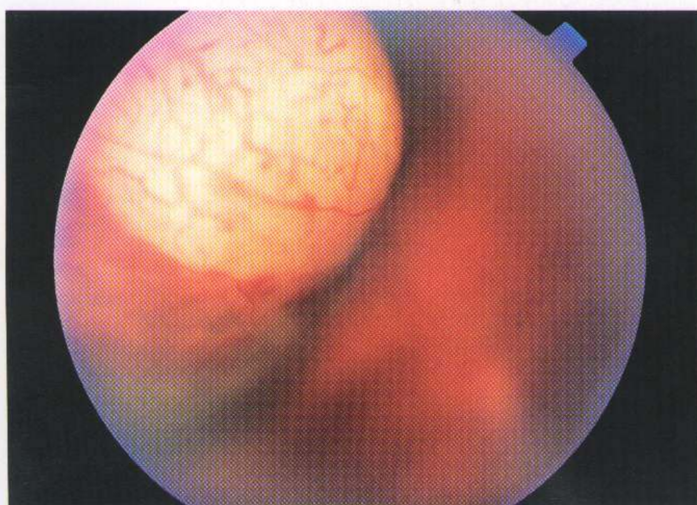


Fig. 11.26
Amelanotic choroidal melanoma

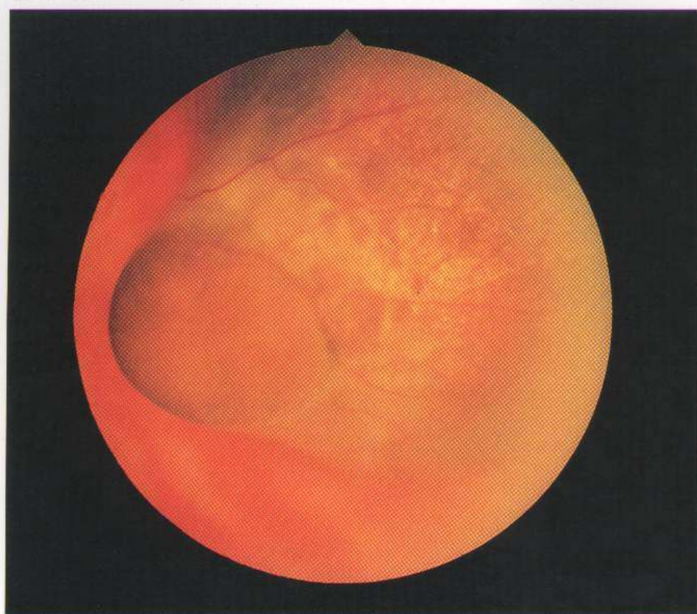


Fig. 11.27
Mushroom-shaped choroidal melanoma with surface lipofuscin (Courtesy of D. Lehman)

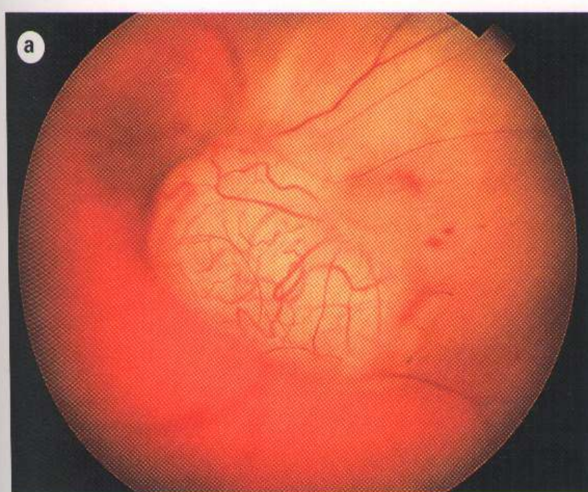


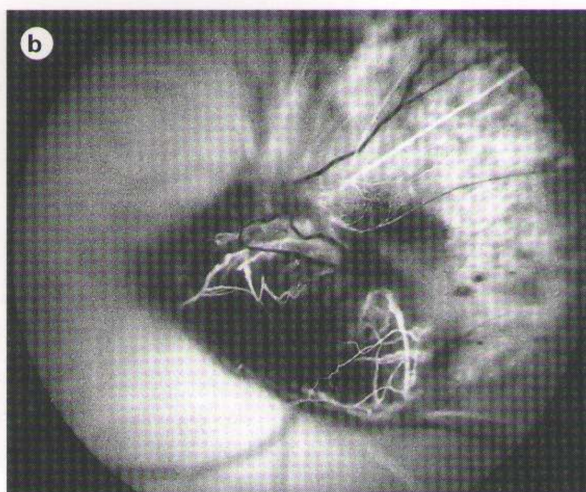
Fig. 11.28
B-scan ultrasonogram showing a choroidal melanoma and secondary retinal detachment

- A secondary exudative detachment is common and must not be mistaken for a rhegmatogenous detachment.
- Occasional features include choroidal folds, haemorrhage, secondary glaucoma, cataract and uveitis.

Investigations

1. **Binocular indirect ophthalmoscopy** is sufficient for accurate diagnosis in the vast majority of cases.
2. **Indirect slit-lamp biomicroscopy** detects subtle features associated with relatively small tumours, such as the presence of lipofuscin pigment, subretinal fluid, cystoid changes in the overlying sensory retina and dilated vessels within the tumour.
3. **Ultrasonography** is used to determine tumour size and detect extraocular extension. B-scan ultrasonography shows the anterior border of the tumour as well as acoustic hollowness, choroidal excavation and orbital shadowing (Fig. 11.28).
4. **FA** is of limited diagnostic value because there is no pathognomonic pattern. Most melanomas show a 'dual circulation' (Fig. 11.29b and c), mottled fluorescence during the arteriovenous phase and progressive leakage and staining (Fig. 11.29d).
5. **ICG** is superior to FA because there is less interference caused by RPE changes, better visualization of the tumour and choroidal vessels, and superior definition of tumour margins.
6. **MRI**, particularly when combined with surface coils and fat suppression sequences, shows that choroidal melanomas are hyperintense in T1-weighted (Fig. 11.30) and hypointense in T2-weighted images, but these features are not pathognomonic.
7. **Colour-coded Doppler** imaging may differentiate pigmented tumours from intraocular haemorrhage, particularly in eyes with opaque media.
8. **Fine-needle aspiration biopsy** is used occasionally to obtain cellular aspirates for analysis where the diagnosis cannot be established by less invasive methods.





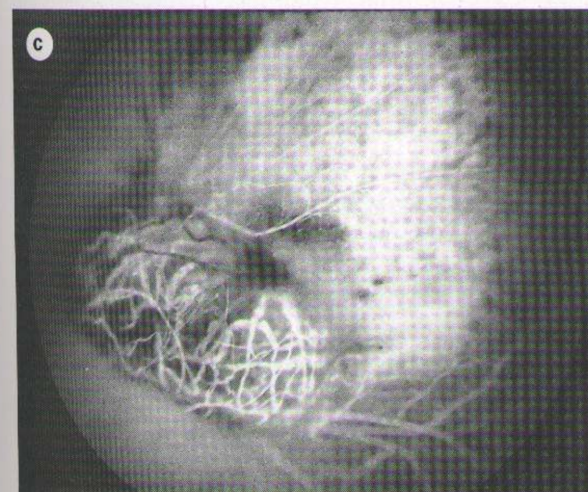




Fig. 11.29
(**a**) Choroidal melanoma; (**b** and **c**) FA early phases showing a 'dual circulation'; (**d**) late phase showing mild hyperfluorescence due to leakage (Courtesy of S. Milewski)

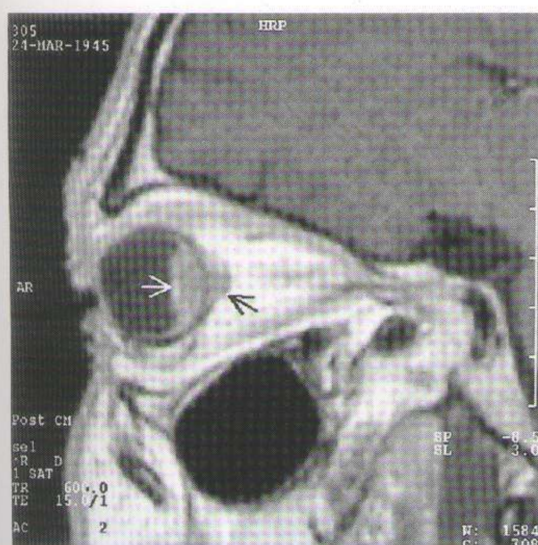


Fig. 11.30
T1-weighted MRI scan showing a choroidal melanoma (white arrow) and extraocular extension (black arrow) (Courtesy of M. Karolczak-Kulesza)

9. **General medical examination** is aimed at:
   - Excluding a metastasis *to* the choroid, which occurs most frequently from the bronchus in both sexes and the breast in women. Occasionally, the primary site is the kidney or gastrointestinal tract. Initial investigations should include chest radiography, rectal examination and mammography in females.
   - Detecting metastatic spread *from* the choroid as this would influence management. For example, a patient with overt metastatic disease would not be subjected to enucleation of a painless eye. The liver is by far the most frequent site for metastases. Hepatic involvement can be detected by ultrasonography and elevated gamma-glutamyl transpeptidase and alkaline phosphatase levels. Chest radiography should also be performed to detect possible lung secondaries but these are rare without liver metastases.

Treatment

This is complex and should be tailored to the individual patient. The following factors are considered: (a) size, location, extent and apparent activity of the tumour, (b) state of the fellow eye, (c) general health and age of the patient and (d) the patient's wishes and fears. For instance, treatment may be inappropriate for a slowly growing tumour in the only eye of a very elderly or chronically ill patient. There is an increasing trend towards the use of combined therapy with the following modalities:

1. **Brachytherapy** is frequently the treatment of first choice because it is relatively straightforward and effective.
   a. *Indications* are tumours less than 10 mm in elevation and less than 20 mm in basal diameter in which there is a reasonable chance of salvaging vision. Supplemental transpupillary thermotherapy may be required to enhance the results. Tumour regression starts about 1–2 months after treatment and continues for several years.
   b. *Complications* include retinopathy, papillopathy, vitreous haemorrhage, cataract and recurrence of tumour.
   c. *Cure rate* is similar to that following enucleation of comparable tumours.
2. **External radiotherapy** with protons or helium ions by means of a cyclotron unit. The advantages over brachytherapy are that the beam can be more highly focused, affording a more homogeneous dose of radiation. Treatment is fractionated over 4 days, with each dose delivered over a 30-second period.
   a. *Indications* are tumours unsuitable for brachytherapy either because of size or posterior location to within 4 mm of the disc or fovea.
   b. *Complications*, which are more common following treatment of large tumours, include loss of lashes, eyelid depigmentation, canaliculitis with epiphora, conjunctival keratinization, keratitis, exudative retinal detachment and neovascular glaucoma.
   c. *Cure rate* is similar to that following brachytherapy or enucleation.
3. **Transpupillary thermotherapy** (TTT) is performed with a diode laser to induce hyperthermia but not coagulation.
   a. *Indications* are selected small tumours, particularly if pigmented and located near the fovea or optic disc. TTT is also a complementary modality to brachytherapy.
   b. *Complications* include visual field defects and maculopathy.
4. **Trans-scleral local resection** is a difficult procedure which involves excision of the tumour with a rim of healthy choroid under a partial-thickness scleral flap. The procedure is performed under systemic arterial hypotension.
   a. *Indications* are carefully selected tumours that are too thick for radiotherapy and usually less than 16mm in diameter.
   b. *Complications* include haemorrhage, retinal detachment, cataract and tumour recurrence.
5. **Stereotactic radiosurgery** with the Gamma-knife is a new method involving single-session delivery of ionizing radiation to a stereotactically localized volume of tissue. This modality is an alternative to charged particle irradiation or enucleation in treating large tumours with preservation of visual function in selected cases.
6. **Enucleation**
   a. *Indications* for excision of the globe are very large tumours, particularly if all useful vision has been irreversibly lost. In these cases, enucleation is preferred to brachytherapy because the dose of radiation required to reach the apex of the tumour would be too great to salvage the rest of the globe.
   b. *Technique* should be meticulous to avoid dissemination of malignant cells. The procedure should be performed with gentle isolation and section of the extraocular muscles, and minimal traction on the optic nerve when cutting. About 4 weeks after enucleation, the patient can be fitted with an artificial eye.
7. **Exenteration** of the orbit is indicated for patients with extensive extraocular extension at the time of diagnosis or for orbital recurrences following enucleation.
8. **Palliation** with chemotherapy and/or immunotherapy may prolong life in patients with metastatic disease. In patients with lung metastases, life expectancy is generally <1 year and, when the liver is involved, <6 months.

Modified Callender classification of uveal melanomas

1. **Spindle cell melanomas**, which make up 45% of all tumours, are composed of spindle cells, with a small proportion described as fascicular because of the palisading or ribbon-like arrangement of cells in parallel rows (Fig. 11.31).
2. **Pure epithelioid cell melanomas** make up 5% (Fig. 11.32).
3. **Mixed cell melanomas**, containing spindle and epithelioid cells, account for 45% (Fig. 11.33).
4. **Necrotic melanomas**, in which the predominant cell type is unrecognizable, make up the remaining 5% (Fig. 11.34).

Prognostic factors

1. **Histological features** implying an adverse prognosis include large numbers of epithelioid cells per high-power field, closed vascular loops within the tumour and lymphocytic infiltration.

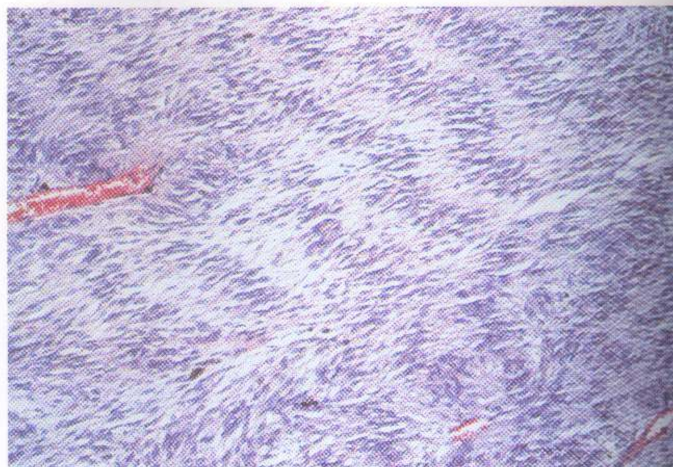
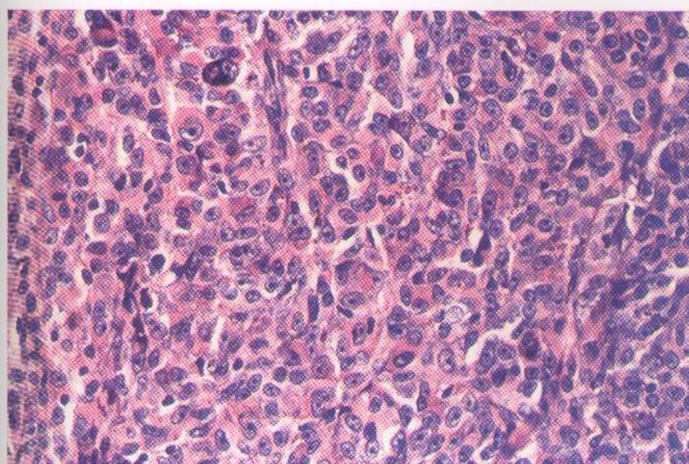
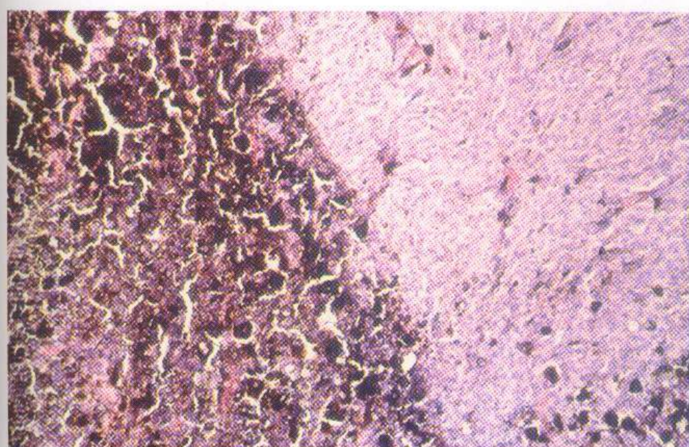
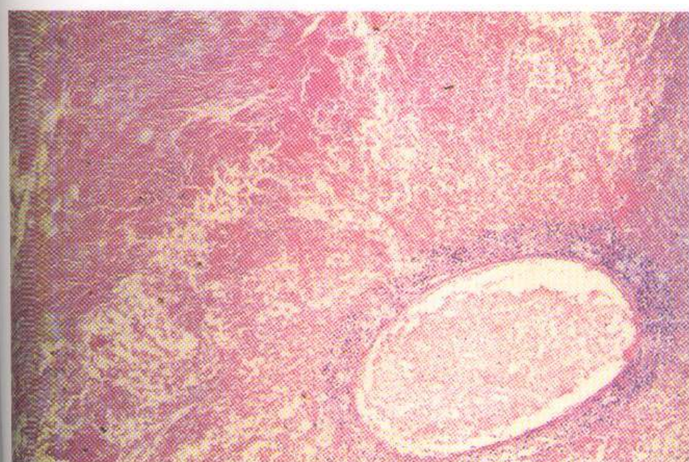


Fig. 11.31
Fascicular spindle cell melanoma (Courtesy of A. Garner)


Fig. 11.32
Epithelioid cell melanoma (Courtesy of A. Garner)


Fig. 11.33
Mixed cell melanoma (Courtesy of A. Garner)


Fig. 11.34
Necrotic melanoma (Courtesy of A. Garner)

2. **Chromosomal abnormalities** within the melanoma cells are associated with a very poor prognosis, with a 50% death rate at 5 years.
3. **Large tumours** have a worse prognosis than small tumours. Following enucleation, 5-year mortality is as follows:
   - Small tumours (<10 mm in diameter): 16%.
   - Medium tumours (10–15 mm in diameter): 32%.
   - Large tumours: 53%.
4. **Extrascleral extension** carries a very poor prognosis.
5. **Location**: anterior tumours have a worse prognosis because they are usually diagnosed later than those near the posterior pole.
6. **Patients over the age of 65 years** have a worse prognosis than younger patients.

Differential diagnosis

Although in the vast majority of cases the diagnosis is straightforward, the following conditions should be considered in the differential diagnosis of atypical cases, particularly amelanotic melanomas:

1. **Other choroidal tumours**, most notably large naevi, circumscribed haemangiomas and solitary metastases.
2. **Solitary choroidal granulomas** associated with sarcoidosis or tuberculosis.
3. **Posterior scleritis** (*see* Chapter 7).

Choroidal naevus

Choroidal naevi are present in about 5% of the general population but are less common in fair-skinned individuals. Although they are probably present at birth, growth occurs mainly during the pre-pubertal years and is extremely rare thereafter. For this reason the rare event of clinically detectable growth should arouse suspicion of malignant transformation.

Signs

1. **Typical naevus**
   - An asymptomatic, oval or circular, slate-blue or green-grey lesion with detectable but not sharp borders which may be associated with surface drusen (Fig. 11.35 and *see* Fig. 11.38a).
   - Dimensions are <5 mm in diameter and 1 mm or less in thickness.
2. **A suspicious naevus** has one or more of the following characteristics:
   - Presence of symptoms, such as metamorphopsia or photopsia.
   - Dimensions >5 mm in diameter and >1 mm in thickness (Fig. 11.36).
   - Clumps of surface orange (lipofuscin) pigment (Fig. 11.37).
   - Absence of surface drusen on a thick lesion.
   - Location of the posterior margin of the lesion within 3 mm of the optic disc.
   - Serous retinal detachment either over the surface of the lesion or inferiorly.

> ***NB:*** The greater the number of these features, the higher the chance that the lesion is a melanoma.

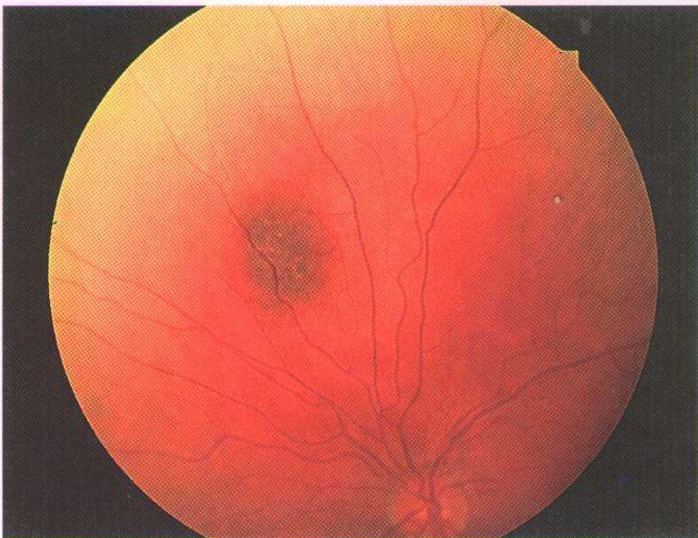


Fig. 11.35
Typical choroidal naevus

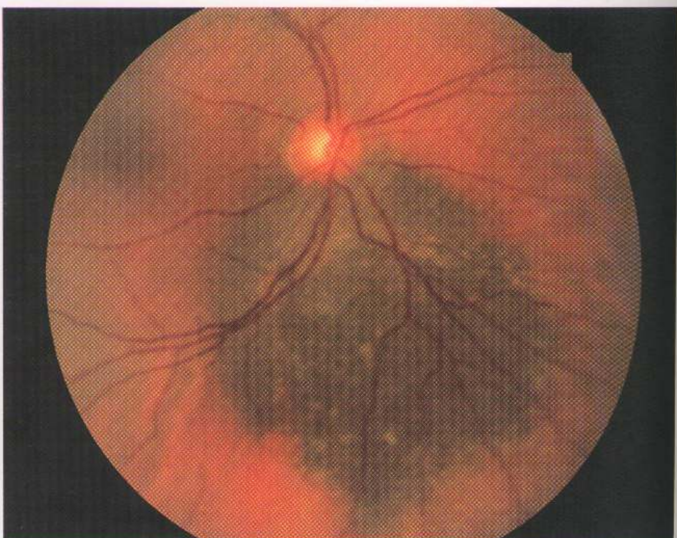


Fig. 11.36
Suspicious choroidal naevus

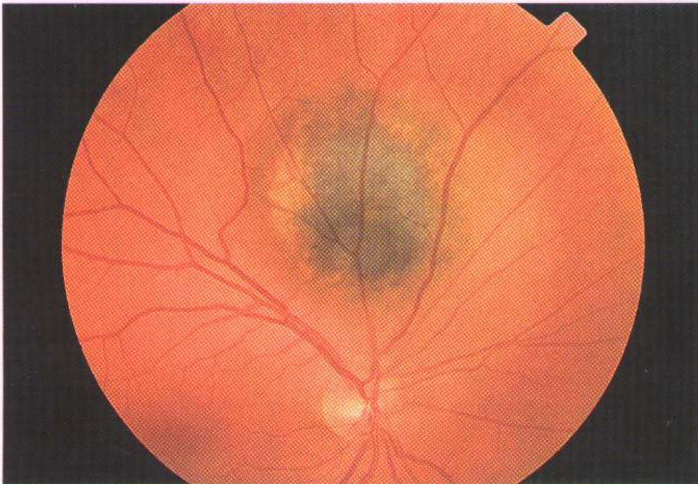
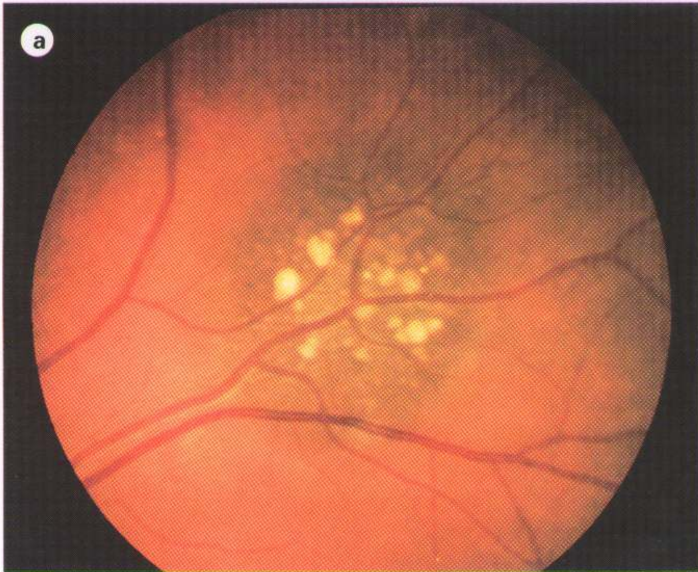


Fig. 11.37
Suspicious choroidal naevus with surface lipofuscin

Investigations

1. **FA** findings depend on the amount of pigmentation within the naevus and associated changes in the overlying RPE. Most choroidal naevi are avascular and pigmented, giving rise to hypofluorescence caused by blockage of background choroidal fluorescence. If the naevus is associated with surface drusen, this will result in areas of hyperfluorescence (Fig. 11.38b). FA is, however, not helpful in distinguishing a small melanoma from a naevus.
2. **Ultrasonography** shows a localized flat or slightly elevated lesion with high internal reflectivity (Fig. 11.39).



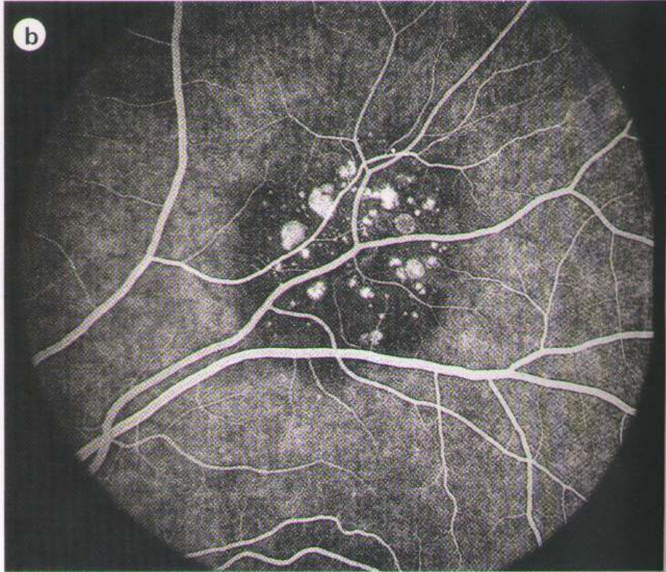


Fig. 11.38
(**a**) Typical choroidal naevus with surface drusen; (**b**) FA showing blockage of background fluorescence and hyperfluorescence of surface drusen



Fig. 11.39
B-scan ultrasonogram of choroidal naevus (*see text*) (Courtesy of M. Karolczak-Kulesza)

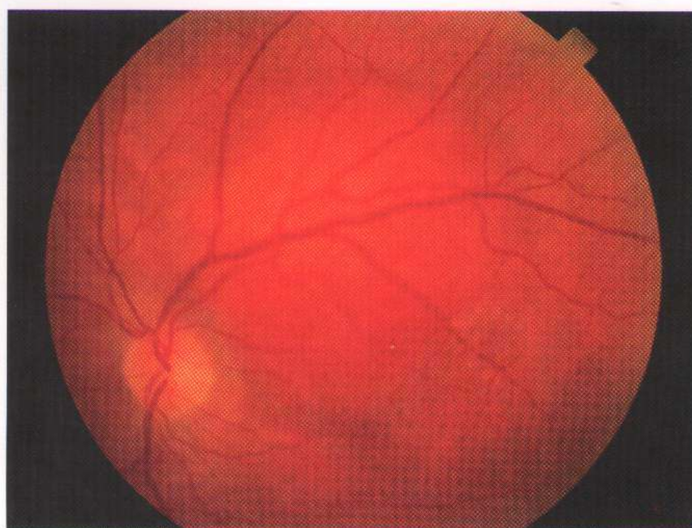


Fig. 11.40
Circumscribed choroidal haemangioma (Courtesy of J.A. Shields and A. Singh)

Management

1. **Typical naevi** do not require follow-up because the risk of malignant transformation is extremely low.
2. **Suspicious naevi** should be evaluated initially every 3–6 months and then 9–12 months with fundus photography and ultrasonography to detect the possibility of growth. Although it is difficult to detect small changes in thickness by ultrasonography, careful comparison of fundus photographs, with special attention to the location of landmarks such as blood vessels, is usually a reliable method of documenting growth. Once growth has been documented, the lesion should be reclassified as a choroidal melanoma and managed accordingly.

Circumscribed choroidal haemangioma

Circumscribed choroidal haemangioma is a rare, benign, vascular hamartoma which is probably present at birth but does not become symptomatic until years later. The tumour is almost always solitary and is not associated with systemic disease. Most are stationary and a few are slow-growing.

Clinical features

1. **Presentation** is in the fourth to fifth decades with unilateral central visual impairment.
2. **Signs**
   - A dome-shaped or placoid, orange-red, mass which blends with the surrounding choroid (Fig. 11.40). Subtle white foci may be present on the surface of the tumour and probably represent fibrous metaplasia of the overlying RPE.
   - The lesion usually measures 3–9 mm in diameter and is most commonly located in the juxtapapillary or macular area.
3. **Complications** include secondary cystoid retinal degeneration overlying the tumour, exudative retinal detachment, macular invasion, RPE degeneration and subretinal fibrosis.

Special investigations

1. **Ultrasonography** shows an oval or placoid lesion with a sharp anterior border and high internal reflectivity, but no choroidal excavation or orbital shadowing (Fig. 11.41).
2. **FA** reveals filling during the choroidal phase (Fig. 11.42a), progressive hyperfluorescence during the venous phase and late leakage (Fig. 11.42b).

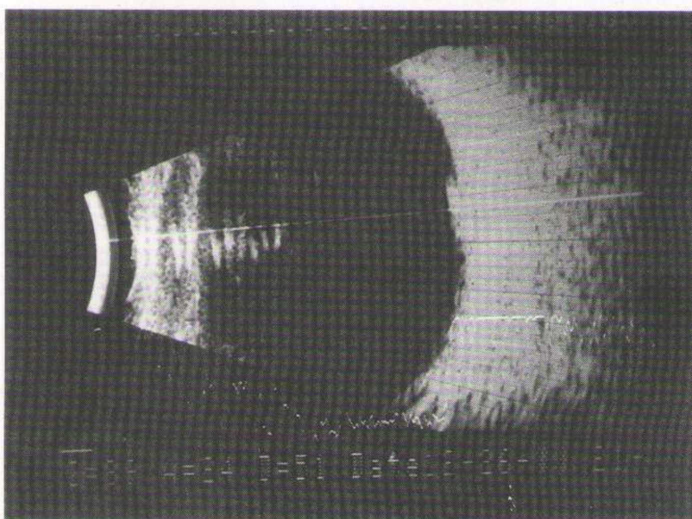
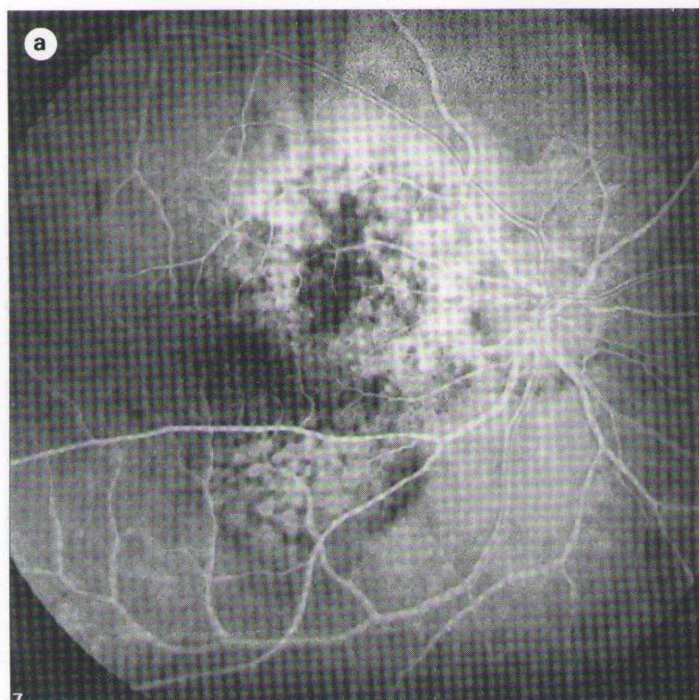


Fig. 11.41
B-scan ultrasonogram of circumscribed choroidal haemangioma (*see text*) (Courtesy of S. Milewski)



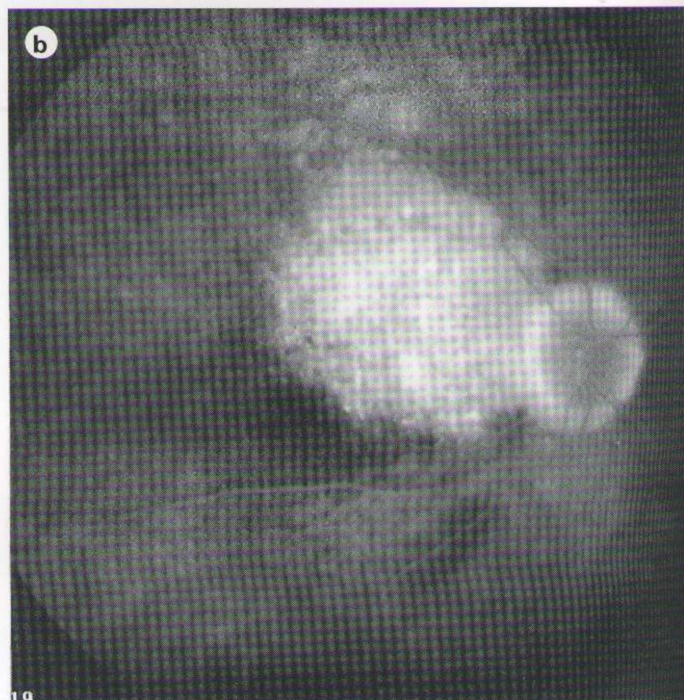


Fig. 11.42
FA of circumscribed choroidal haemangioma. (**a**) Early phase showing hyperfluorescence due to filling; (**b**) late phase showing leakage (Courtesy of S. Milewski)

Treatment

Vision-threatening lesions may be treated as follows:

1. **Transpupillary thermotherapy** for lesions not involving the macula. Indocyanine green can be administered as an adjunct to enhance uptake of diode laser energy.
2. **Radiotherapy** either by low-dose lens-sparing external beam irradiation or brachytherapy.

Diffuse choroidal haemangioma

The diffuse choroidal haemangioma usually affects over half of the choroid and enlarges very slowly. It occurs in patients with the Sturge–Weber syndrome ipsilateral to the naevus flammeus (*see* Chapter 20).

1. **Presentation** is in the third decade with visual impairment.
2. **Signs**. Thickening of the choroid and a deep-red 'tomato ketchup' colour which is most marked at the posterior pole (Fig. 11.43).
3. **Complications** include secondary retinal cystoid degeneration and exudative retinal detachment.
4. **Treatment** is by external beam radiotherapy.

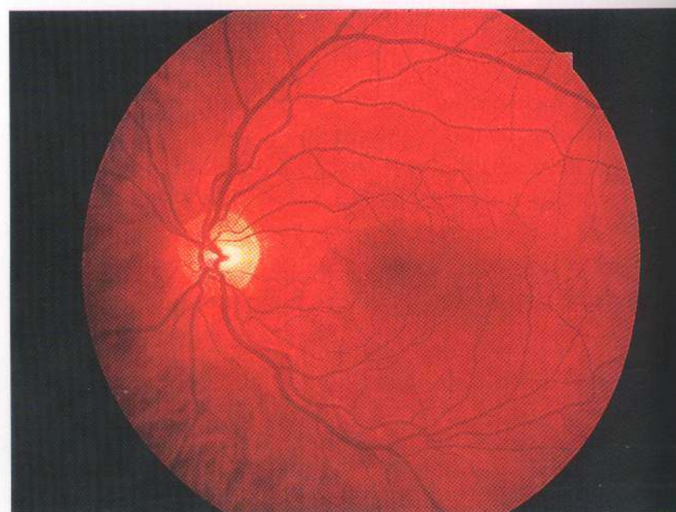


Fig. 11.43
Diffuse choroidal haemangioma

Metastatic tumours

The choroid is by far the most common site for uveal metastases, accounting for about 90%, followed by the iris and ciliary body. Metastatic tumours to the choroid are more common than primary malignancies but their presence is *usually undetected or overshadowed by the patient's general* illness. The most frequent primary site is the breast in women and the bronchus in both sexes. A choroidal secondary may be the initial presentation of a bronchial carcinoma, whereas a past history of breast cancer is the rule in patients with breast secondaries. Other less common primary sites include the gastrointestinal tract, kidney and skin melanoma. The prostate is, however, an extremely rare primary site. Patient survival is generally poor, with a median of 8–12 months for all patients and 15–17 months for those with breast carcinoma. In patients with breast carcinoma risk factors for choroidal metastases include dissemination of disease in more than one organ and *the presence of lung and brain metastases.*

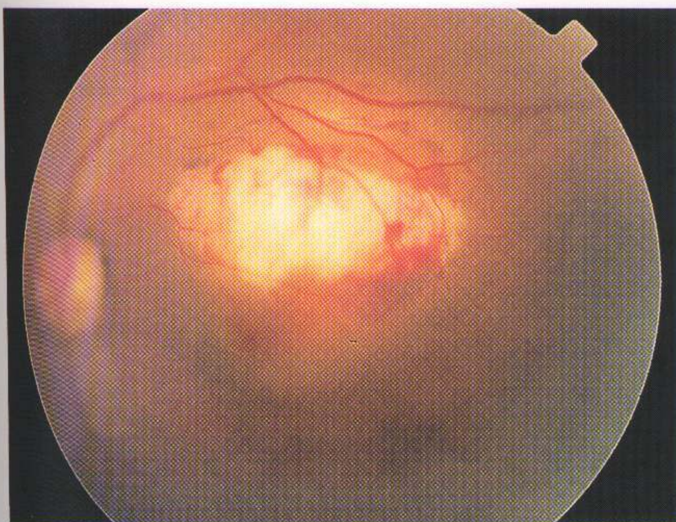


Fig. 11.44
Choroidal metastasis from colon carcinoma (Courtesy of S. Milewski)

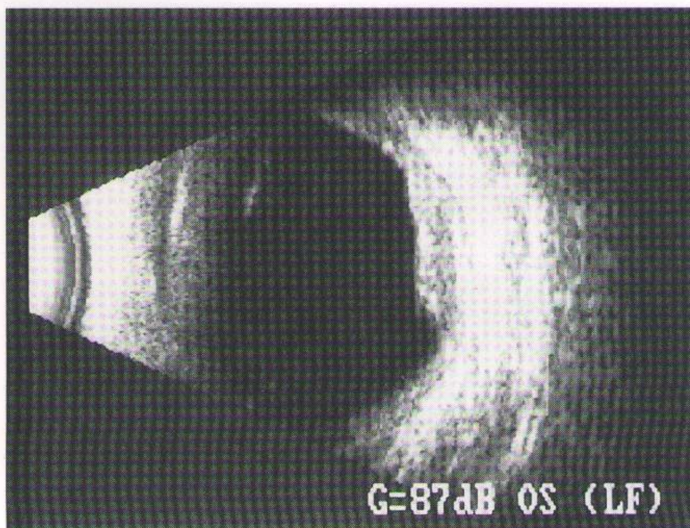


Fig. 11.46
Ultrasonogram of choroidal metastasis (*see text*) (Courtesy of M. Karolczak-Kulesza)

Clinical features

1. **Presentation** is usually with visual impairment although metastases may be asymptomatic if located away from the macula.
2. **Signs**
   - A fast-growing, creamy-white, placoid or oval lesion most frequently located at the posterior pole (Fig. 11.44).
   - The tumour seldom becomes significantly elevated because it infiltrates laterally (Fig. 11.45).
   - Occasionally the deposits assume a globular shape and may mimic an amelanotic melanoma.
   - The deposits may be multiple and both eyes are involved in 10–30% of cases.
   - Secondary exudative retinal detachment is frequent and may occur in eyes with relatively small deposits.

Special investigations

1. **Ultrasonography** shows diffuse choroidal thickening and moderate internal acoustic reflectivity (Fig. 11.46).
2. **FA** shows early hyperfluorescence (Fig. 11.47b) with diffuse late staining (Fig. 11.47c and d) but in contrast with choroidal melanomas a 'dual circulation' does not occur.

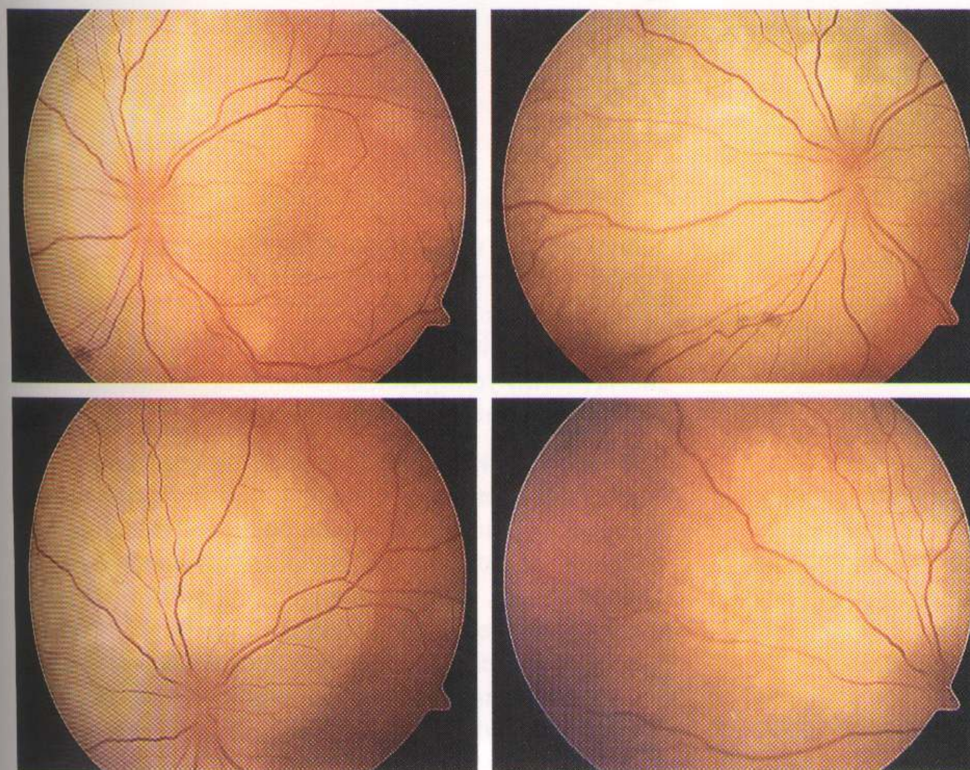


Fig. 11.45
Choroidal metastasis from breast carcinoma (Courtesy of M. Karolczak-Kulesza

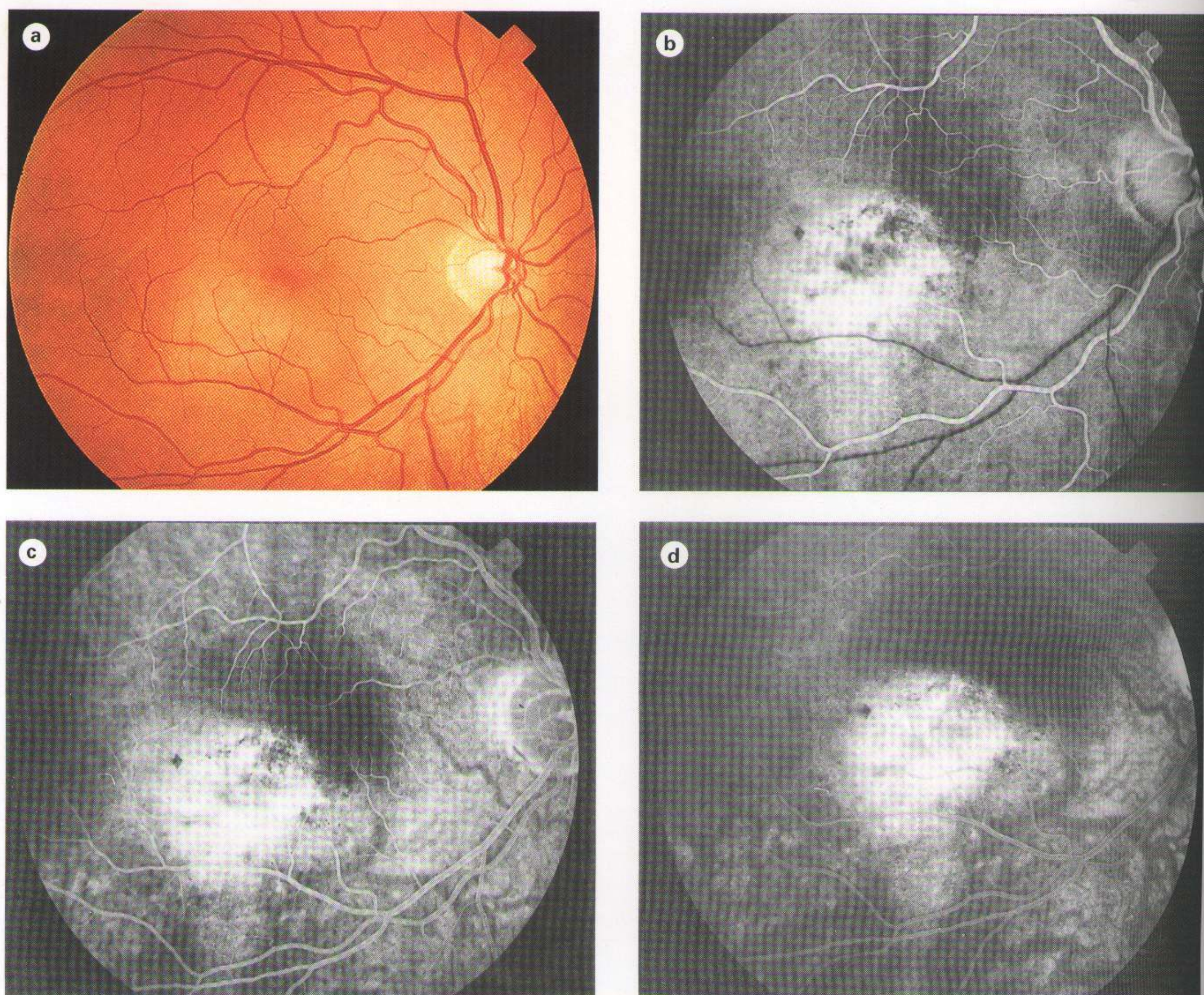


Fig. 11.47
(**a**) Choroidal metastasis; (**b**) FA arterial phase showing hyperfluorescence but absence of a 'dual circulation'; (**c, d**) late phases showing staining (Courtesy of S. Milewski)

3. **Biopsy**, performed either trans-sclerally or by fine-needle aspiration, may be useful.
4. **Systemic** investigations to detect the primary tumour, if unknown, or other metastatic sites.

Treatment

1. **Observation**, if the patient is asymptomatic or receiving systemic chemotherapy.
2. **Radiotherapy**, either external beam or brachytherapy, for small tumours.
3. **Transpupillary thermotherapy** is useful for deposits of moderate thickness and minimal amount of subretinal fluid.
4. **Systemic therapy** for the primary tumour may be beneficial for choroidal metastases.
5. **Enucleation** may be required for a painful blind eye.

Choroidal osseous choristoma

Choroidal osseous choristoma (osteoma) is a very rare, benign, very slow-growing, ossifying tumour which typically affects healthy young women. Both eyes are affected in about 25% of cases but not usually simultaneously.

1. **Presentation** is in the second to third decades with gradual visual impairment if the macular is involved.
2. **Signs**. An orange-yellow lesion with well-defined scalloped borders, most commonly situated at the posterior pole (Fig. 11.48). The tumour grows very slowly with the development of overlying RPE changes (Fig. 11.49).
3. **Complications**. Secondary choroidal neovascularization is common and responds poorly to laser photocoagulation.
4. **FA** shows a diffuse mottled pattern of hyperfluorescence during the early and late phases.

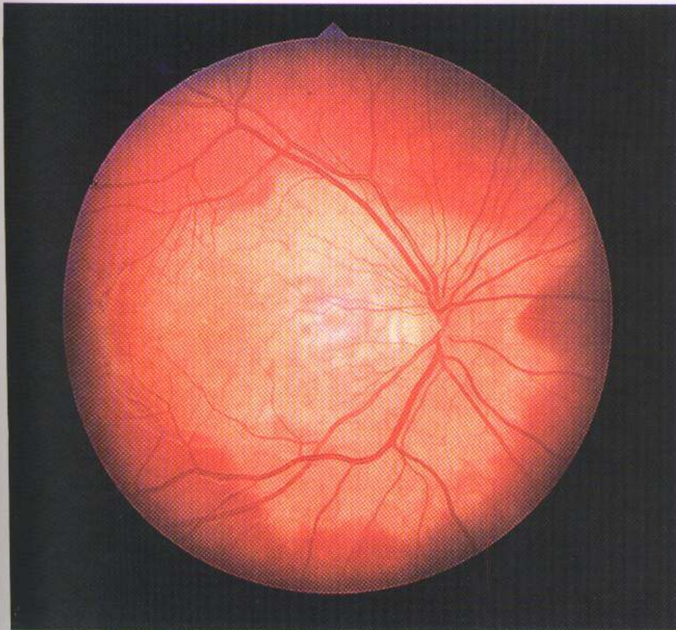


Fig. 11.48
Choroidal osseous choristoma

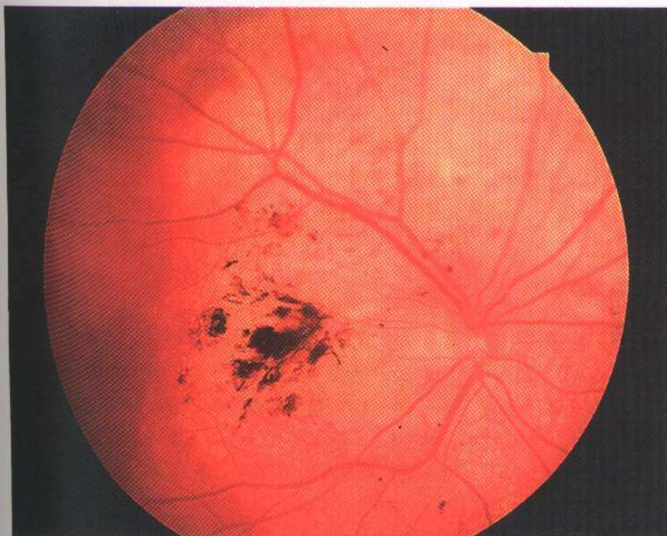


Fig. 11.49
Same eye several years later showing overlying RPE changes

5. **Ultrasonography** shows a very dense highly reflective lesion (bone) which renders silent the orbital tissue behind it (Fig. 11.50).

Melanocytoma

Melanocytoma is a benign, heavily pigmented tumour that may occur anywhere in the uveal tract, but arises most frequently from dendritic uveal melanocytes in the lamina cribrosa of the optic nerve head. Anterior uveal melanocytomas may undergo acute necrosis with resultant uveitis, pigment dispersion and secondary glaucoma. In contrast with choroidal melanoma, melanocytoma typically affects dark-skinned individuals, although it may also occur in white people.

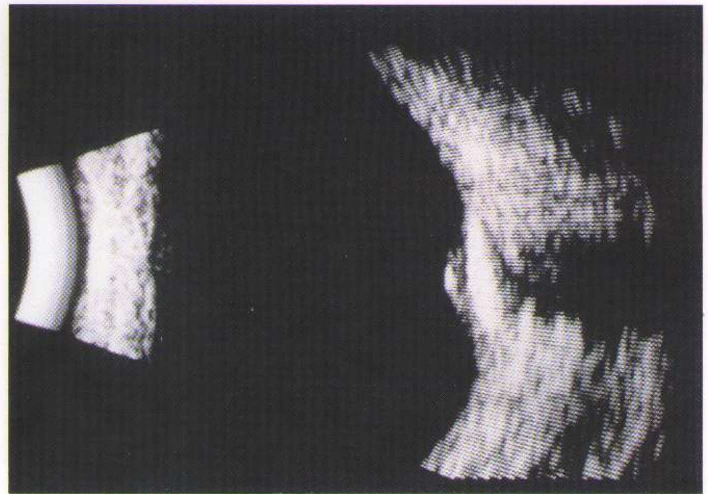


Fig. 11.50
Ultrasonogram of choroidal osseous choristoma (*see text*)

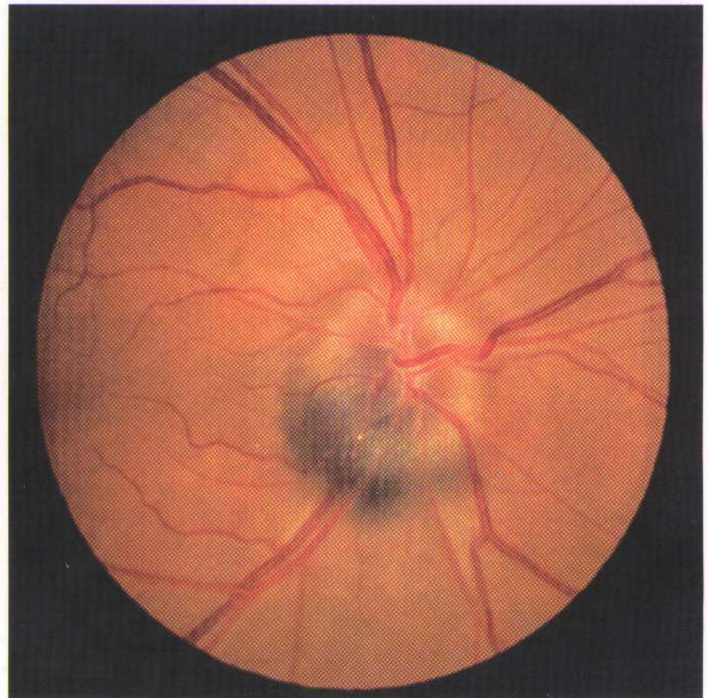


Fig. 11.51
Melanocytoma of the optic nerve head

1. **Presentation** of optic nerve head melanocytoma is usually by chance, although a deep-seated tumour may cause optic nerve dysfunction.
2. **Signs**. A black lesion with feathery edges frequently occupying the inferior part of the disc (Fig. 11.51). Occasionally, the tumour is elevated and occupies the entire disc surface.
3. **Complications**, which are rare, include malignant transformation and central retinal vascular obstruction secondary to spontaneous tumour necrosis.
4. **Treatment** is not required except in the very rare event of malignant transformation.
5. **Differential diagnosis** includes choroidal melanoma invading the optic nerve head and reactive RPE hyperplasia.

Lymphoma

Primary intraocular–central nervous system lymphoma is an uncommon, diffuse, highly malignant, large B-cell (non-Hodgkin) lymphoma. It arises within the brain, spinal cord, leptomeninges and/or the eye and has a poor prognosis, with a 5-year survival rate of less than 33%.

CNS features

1. **At presentation** the following four profiles are seen:
   - Solitary or multiple intracranial nodules.
   - Diffuse meningeal or periventricular lesions.
   - Localized intradural spinal masses.
   - Intraocular involvement.
2. **The diagnosis** is usually made by identifying malignant lymphocytes in the brain, cerebrospinal fluid or vitreous.

Ocular features

Lymphoma tends to involve the vitreous and retina and frequently represents a diagnostic challenge, masquerading as uveitis. Ocular findings usually precede CNS involvement by months or a few years and only 20% of patients have ocular lesions at the time of diagnosis of CNS disease. Both eyes are eventually affected in 80% of cases, but the severity of involvement is often asymmetrical.

1. **Chronic anterior uveitis** unresponsive to steroids.
2. **Intermediate uveitis** in an elderly patient may initially be responsive to steroids but subsequently becomes unresponsive. The vitreous typically shows large clumps or sheets composed of malignant cells.
3. **Posterior segment**
   - Multifocal, large, yellowish, sub-RPE infiltrates are most commonly seen (Fig. 11.52). Coalescence of the lesions may form a ring which is pathognomonic for intraocular lymphoma (Fig. 11.53).
   - Less frequent manifestations include diffuse retinal infiltrates resembling viral retinitis, vascular sheathing and occlusion, and multifocal, tiny deep white lesions which can be misdiagnosed as inflammatory.
4. **Investigations** include neurological evaluation, MRI, lumbar puncture and vitreous biopsy.

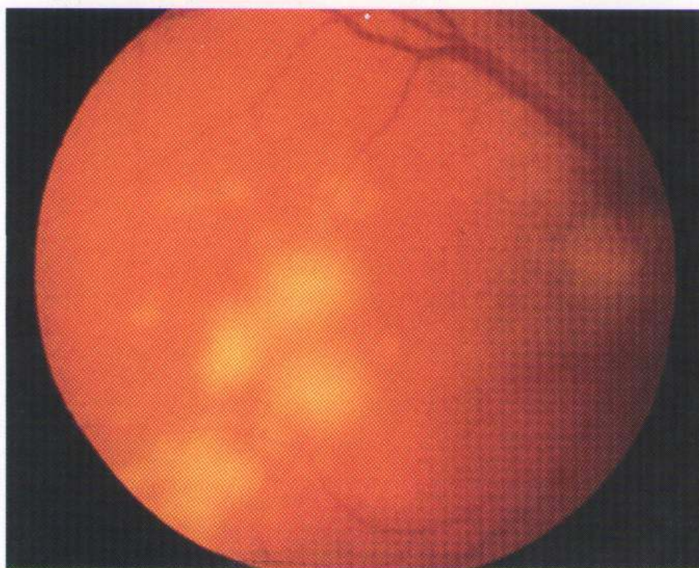


Fig. 11.52
Multifocal lymphomatous subretinal infiltrates (Courtesy of A. Cruess)

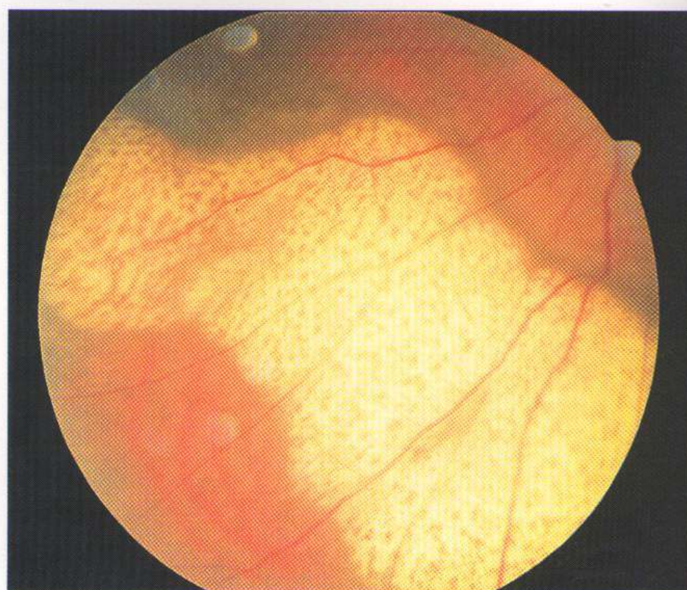


Fig. 11.53
Annular lymphomatous subretinal infiltration (Courtesy of B. Damato)

Treatment

1. **Systemic** treatment is with high-dose external beam radiotherapy to the eyes, sometimes in conjunction with whole brain radiotherapy, and/or systemic or intrathecal chemotherapy.
2. **Intravitreal** methotrexate may be used as primary treatment and for recurrences following systemic therapy.

Retinal and optic nerve head tumours

Retinoblastoma

Retinoblastoma is the most common primary intraocular malignancy of childhood. Even so, it is rare, occurring in about 1:20,000 live births and accounts for about 3% of all childhood cancers.

Genetics

Retinoblastoma results from malignant transformation of primitive retinal cells before final differentiation. Because these cells disappear within the first few years of life, the tumour is seldom seen after 3 years of age. Retinoblastoma

may be heritable or non-heritable. The predisposing gene (*RPE1*) is at 13q14.

1. **Heritable** (germline) retinoblastoma accounts for 40%. In these patients one allele of the *RPE1* (a tumour supressor gene) has mutated in all body cells. When a further mutogenic event ('second hit') affects the second allele, the cell undergoes malignant transformation. Because all the retinal precursor cells contain the initial mutation, these children develop bilateral and multifocal tumours. Familial cases also carry a predisposition to non-ocular cancers; most notably pinealoblastoma (trilateral retinoblastoma) and osteosarcoma. The risk of second malignancy increases greatly if external beam irradiation has been used to treat the original tumour, and the second tumour tends to arise within the irradiated field.
   - The risk of transmitting the gene mutation is 50%, and because of high penetrance 40% of offspring of a survivor of heritable retinoblastoma will develop the tumour.
   - Unaffected parents of a child with bilateral retinoblastoma with no family history have a 40% chance of producing another affected child.
   - Some familial cases present with initially unilateral disease and about 15% of patients with heritable retinoblastoma only express unilateral involvement.
2. **Non-heritable** (somatic) retinoblastoma accounts for 60% of cases. The tumour is unilateral, not transmissible and does not predispose the patient to an increased risk of second non-ocular cancers. Eighty-five per cent of patients with unilateral retinoblastoma fall into this category.

Presentation

The vast majority present within the first 2 years of life. Children with bilateral tumours tend to present earlier (average 12 months) than those with unilateral involvement.

1. **Leukocoria** (white pupillary reflex) is the commonest (60%) (Fig. 11.54).
2. **Strabismus** is the second most common (20%). Fundus examination is therefore mandatory in all cases of childhood strabismus.



Fig. 11.54
Left leukocoria due to advanced retinoblastoma (Courtesy of C. Barry)

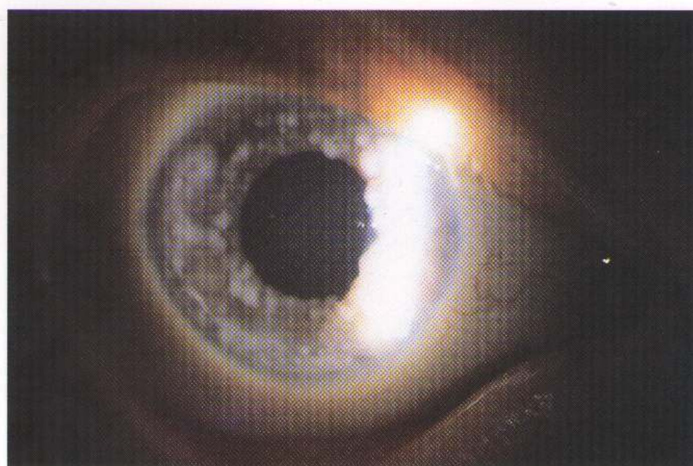


Fig. 11.55
Multiple iris nodules due to invasion by retinoblastoma

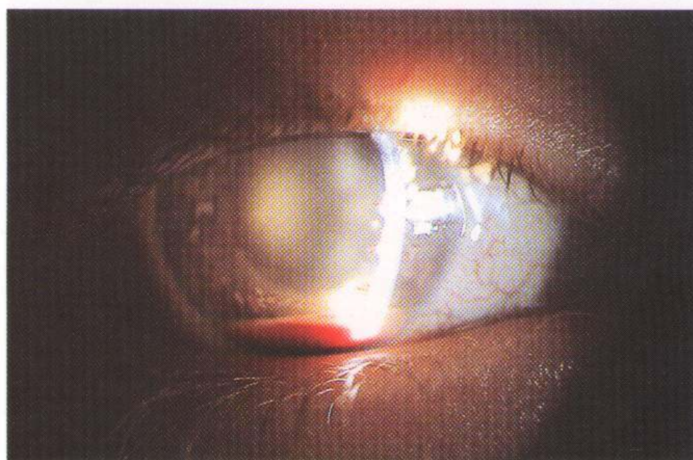


Fig. 11.56
Pseudo-hypopyon due to anterior segment invasion by retinoblastoma

3. **Secondary glaucoma**, sometimes associated with buphthalmos, is uncommon.
4. **Unilateral iris invasion** in older children (average age 6 years) may manifest as multifocal nodules (Fig. 11.55), resembling granulomatous inflammation, or pseudo-hypopyon (masquerade syndrome) (Fig. 11.56). It is therefore important to consider retinoblastoma in the differential diagnosis of unusual chronic uveitis in children.
5. **Orbital inflammation** mimicking orbital or preseptal cellulitis may occur with necrotic tumours (Fig. 11.57). It does not necessarily imply extraocular extension and the exact mechanism is not known.
6. **Orbital invasion** may occur in neglected cases (Fig. 11.58).
7. **Metastatic disease** involving regional lymph nodes and brain before the detection of ocular involvement is rare.
8. **Raised intracranial pressure** due to 'trilateral retinoblastoma' before the diagnosis of ocular involvement is very rare.
9. **On routine examination** of a patient known to be at risk.



Fig. 11.57
Orbital inflammation associated with retinoblastoma



Fig. 11.58
Orbital invasion by neglected retinoblastoma

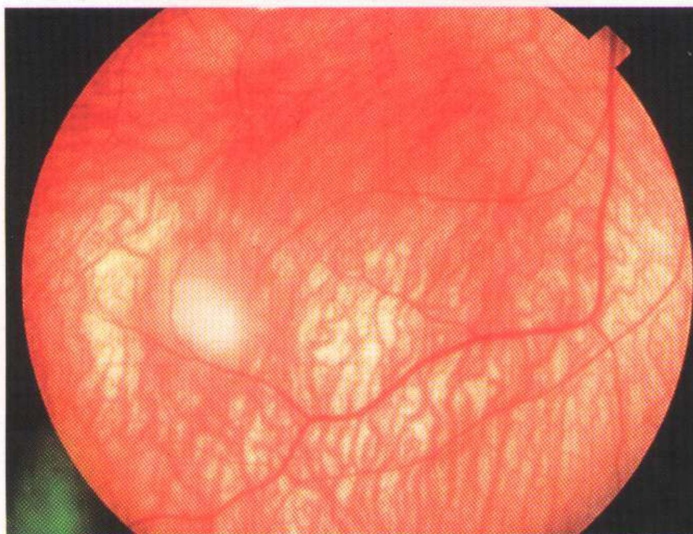


Fig. 11.59
Small intraretinal retinoblastoma

Signs

Indirect ophthalmoscopy with scleral indentation must be performed on *both eyes* after full mydriasis. This is because without indentation pre-equatorial tumours may be missed and one eye may harbour multiple tumours. The clinical signs depend on tumour size and growth pattern.

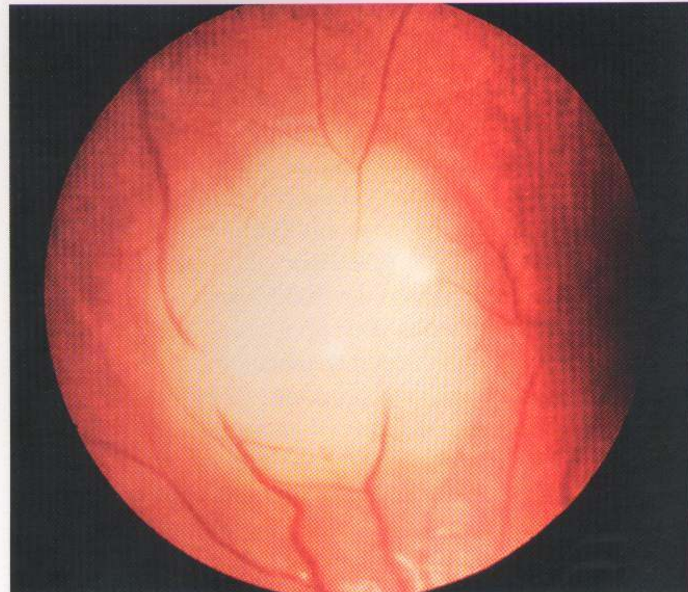


Fig. 11.60
Retinoblastoma

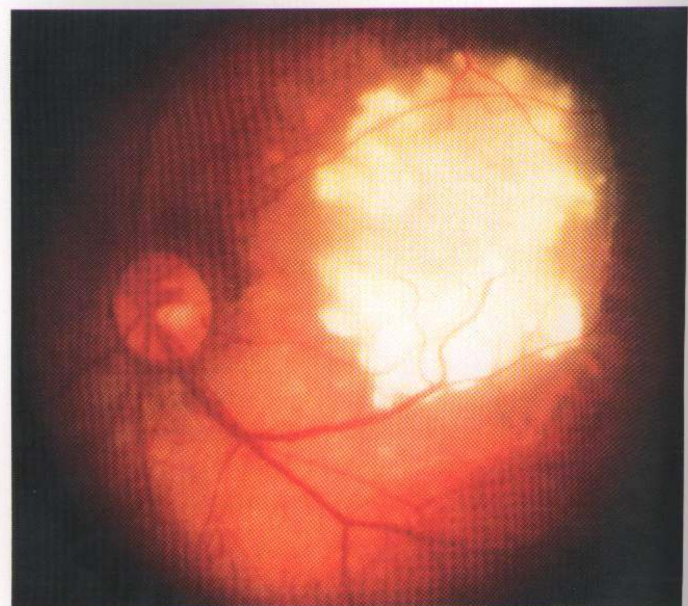


Fig. 11.61
Endophytic retinoblastoma (Courtesy of C. Barry)

1. **An early intraretinal** tumour is a placoid white lesion (Figs 11.59 and 11.60).
2. **An endophytic** tumour grows inwards towards the vitreous, projecting from the retinal surface as a white, cottage cheese-like mass, with surface blood vessels (Fig. 11.61).
3. **An exophytic** tumour grows outwards as a subretinal, multilobulated white mass (Fig. 11.62). It detaches the retina and may be difficult to visualize if the subretinal fluid is deep (Fig. 11.63).



Fig. 11.62
Exophytic retinoblastoma (Courtesy of S. Milewski)

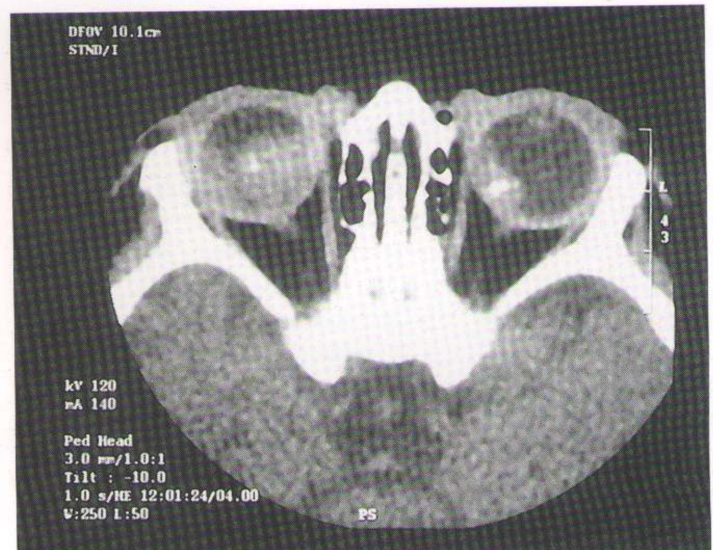


Fig. 11.64
CT scan showing bilateral advanced retinoblastomas (Courtesy of K. Nischal)

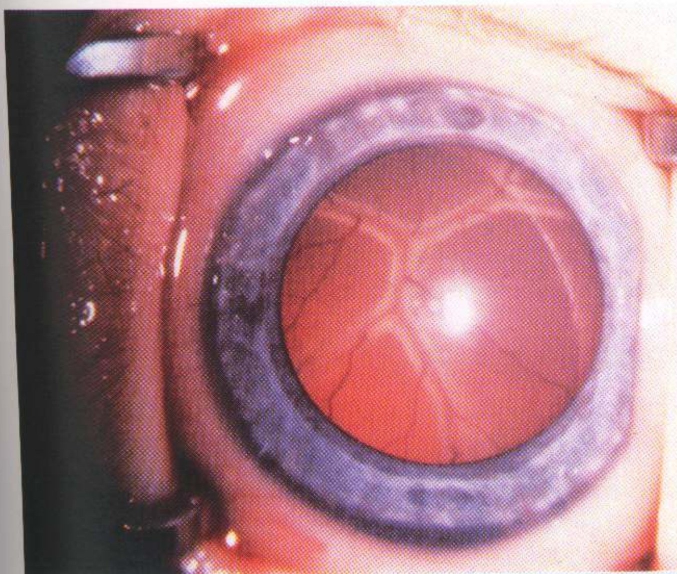


Fig. 11.63
Retinal detachment caused by exophytic retinoblastoma

Special investigations

1. **Ultrasonography** is used mainly to assess tumour size. It also detects calcification within the tumour and is helpful in the diagnosis of simulating lesions such as Coats disease and toxocariasis.
2. **CT** demonstrates gross involvement of the optic nerve, orbital and CNS extension, and the presence of pinealoblastoma and calcification (Fig. 11.64). However, it entails a significant dose of radiation which may be dangerous in patients with germinal mutations.
3. **MRI** cannot detect calcification, but is superior to CT for optic nerve evaluation and detection of a pinealoblastoma, especially when contrast is used. MRI may also be useful to differentiate retinoblastoma from simulating conditions.
4. **Systemic investigations** such as bone marrow aspiration and lumbar puncture are performed only in patients with optic nerve involvement or evidence of extraocular extension.

Treatment

Treatment is related to tumour size, location and associated findings such as retinal detachment, subretinal and vitreous tumour seeds and the state of the fellow eye.

1. **Small tumours**, no more than 4 mm diameter and 2 mm thickness without vitreous or subretinal seeds can be treated with transpupillary thermotherapy laser or cryo-

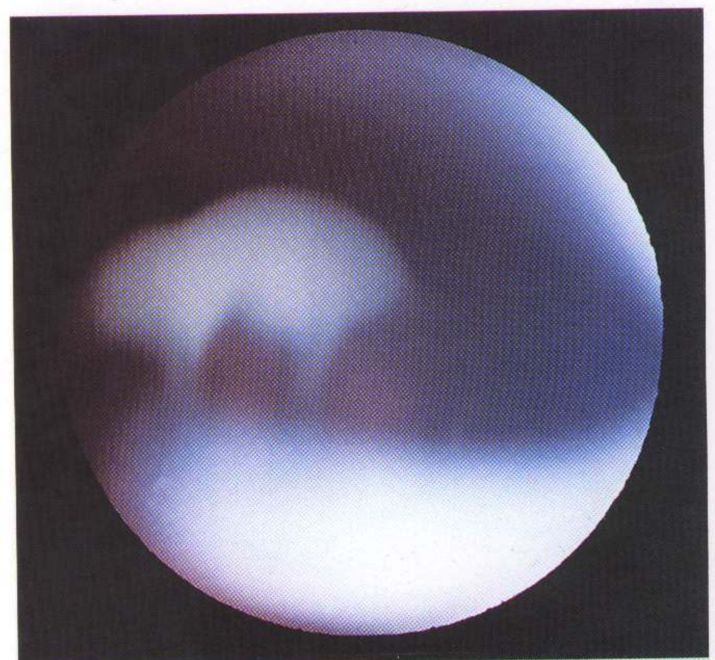


Fig. 11.65
Small peripheral retinoblastoma seen on scleral indentation

therapy. The latter is particularly useful for pre-equatorial tumours which are difficult to reach with laser (Fig. 11.65).

2. **Medium-size tumours**
   a. ***Brachytherapy*** is indicated for tumours of no more than 12 mm diameter and 6 mm thickness, which are unsuitable for thermotherapy or cryotherapy, provided there is no vitreous seeding. Following treatment the tumour regresses leaving a calcific residue (Fig. 11.66).
   b. ***Chemotherapy*** with carboplatin, vincristine and etoposide which may be combined with cyclosporin. The drugs are given intravenously in 3 week cycles over a 4–9 month period depending on disease severity. This may be followed by local treatment with cryotherapy or thermotherapy to consolidate tumour control.

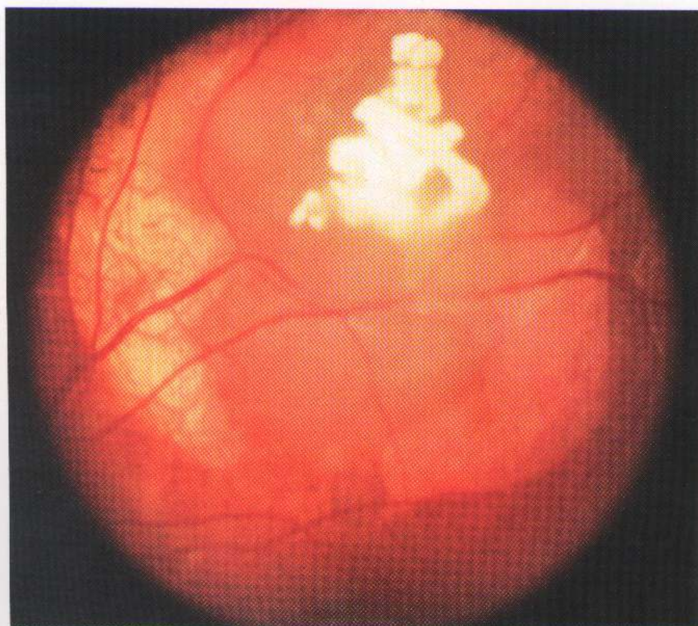


Fig. 11.66
Regressed retinoblastoma with calcific residue

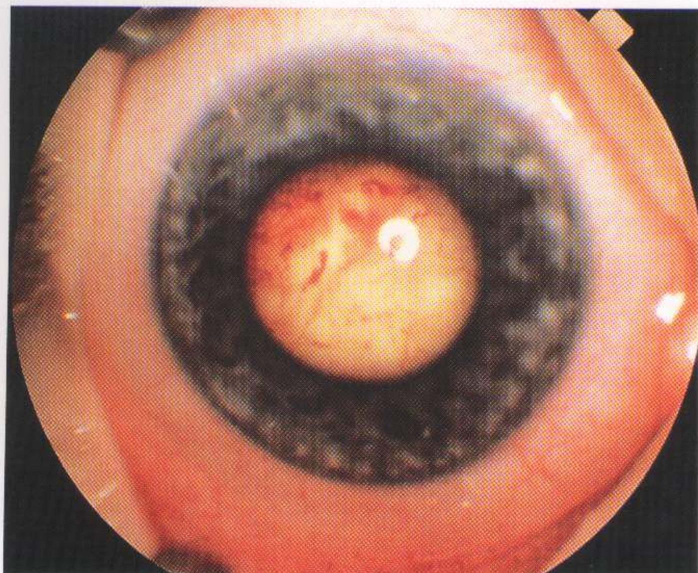


Fig. 11.67
Large retinoblastoma with new surface vessels

   c. ***External beam radiotherapy*** should be avoided, if possible, due to the high risk of complications such as cataract formation, radiation retinopathy and cosmetic deformities. In patients with germinal mutations there is also a risk of inducing a second malignancy such as sarcoma of bone or connective tissue.
3. **Large tumours** (Fig. 11.67)
   a. ***Chemotherapy*** to shrink the tumour (chemoreduction), facilitating subsequent local treatment, thereby avoiding enucleation or external beam radiotherapy. Chemotherapy also will have a beneficial effect if a smaller tumour is present in the fellow eye.
   b. ***Enucleation*** if chemoreduction fails or a normal fellow eye makes aggressive chemotherapy inappropriate. It is also useful for diffuse retinoblastoma because of poor visual prognosis and high risk of recurrence with other therapeutic modalities. Enucleation should be performed with minimal manipulation and it is imperative to obtain a long piece of optic nerve (8–12 mm). There is no contraindication to the insertion of an orbital implant. Unfortunately subsequent shortening of the fornices and retraction of the implant (post-enucleation socket syndrome) may require further surgical intervention.
4. **Extraocular extension** beyond the lamina cribrosa is treated with chemotherapy after enucleation. Extension to the cut end of the optic nerve, or extension through the sclera, is treated with chemotherapy and irradiation of the affected orbit.
5. **Metastatic disease** is treated with high-dose chemotherapy. Patients with malignant cells in the cerebrospinal fluid may require intrathecal methotrexate.

Prognostic factors

The overall mortality rate is 2–5% and is related to the following:

1. **Tumour size and location**. Small posterior tumours do best but there is no significant difference between endophytic and exophytic types.

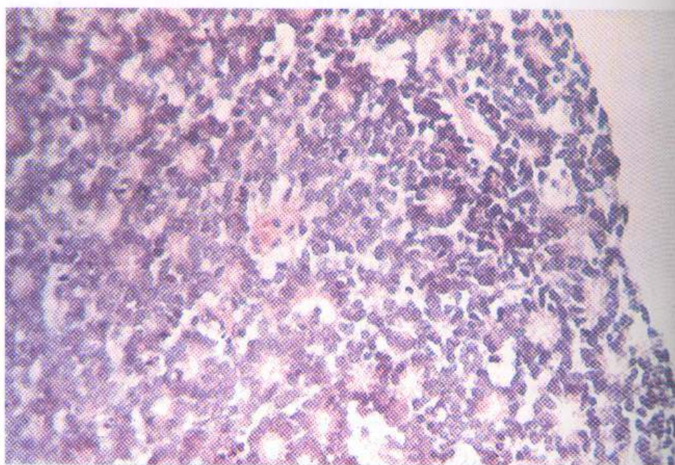
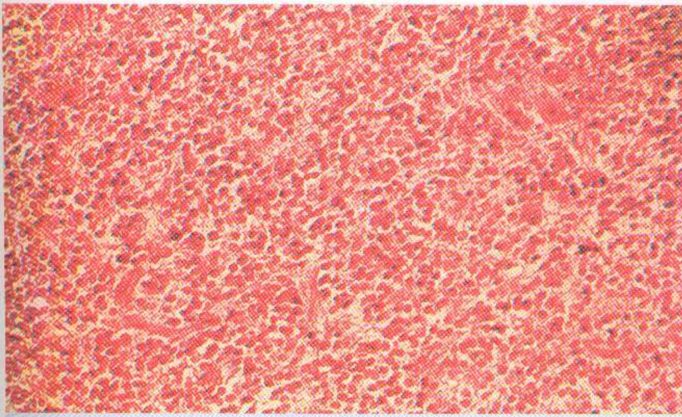


Fig. 11.68
Well-differentiated retinoblastoma with abundant rosettes
(Courtesy of A. Garner)


Fig. 11.69
Highly undifferentiated retinoblastoma (Courtesy of A. Garner)

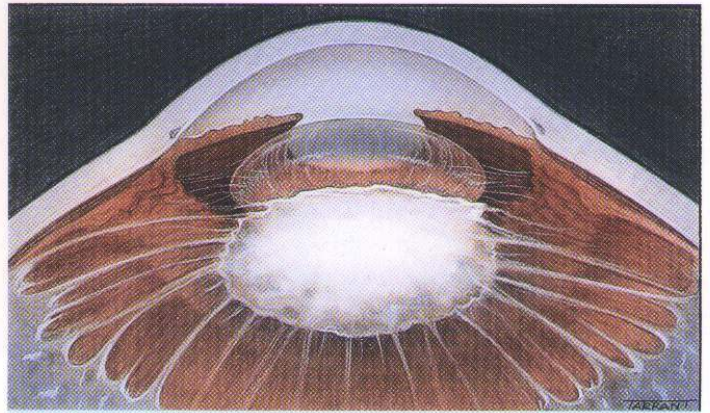
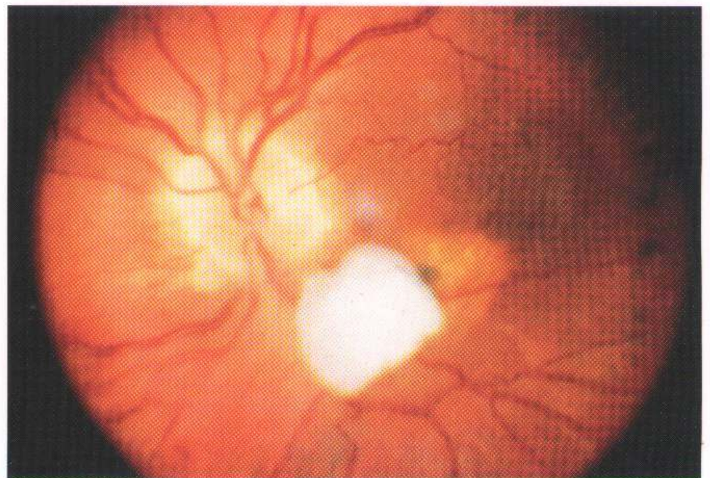

Fig. 11.71
Persistent hyperplastic primary vitreous


Fig. 11.70
Leukocoria associated with persistent hyperplastic primary vitreous


Fig. 11.72
Toxocara granuloma resembling endophytic retinoblastoma

2. **Cellular differentiation**. The mortality rate of patients whose tumours have abundant rosettes (Fig. 11.68) is much less than in those with highly undifferentiated tumours (Fig. 11.69).
3. **Optic nerve involvement** beyond the point of surgical transection is associated with high mortality.
4. **Invasion** of the choroid or vortex veins facilitates haematogenous spread and is therefore of adverse prognostic significance.
5. **Extrascleral spread** carries a grave prognosis.

Differential diagnosis

1. **Persistent hyperplastic primary vitreous** is an important cause of congenital leukocoria (Fig. 11.70). It typically occurs in a microphthalmic eye and is almost always unilateral. It is characterized by a retrolental mass into which elongated ciliary processes are inserted (Fig. 11.71). With time the mass contracts and pulls the ciliary processes centrally so that they become visible through the pupil. An associated dehiscence involving the posterior capsule may lead to subsequent cataract formation.
2. **Coats disease** is almost always unilateral, more common in boys and tends to present later than retinoblastoma. It is characterized by telangiectatic retinal blood vessels, extensive intra- and subretinal yellow exudation and exudative retinal detachment (*see* Chapter 14).
3. **Retinopathy of prematurity**, if advanced, may cause retinal detachment and leukocoria. Diagnosis is usually straightforward because of the history of prematurity and low birth weight (*see* Chapter 14).
4. **Toxocariasis** (*see* Chapter 10).
   a. *Chronic toxocara endophthalmitis* may cause a cyclitic membrane and a white pupil.
   b. *Toxocara granuloma* at the posterior pole may resemble an endophytic retinoblastoma (Fig. 11.72).
5. **Intermediate uveitis** may mimic the diffuse infiltrating type of retinoblastoma seen in older children (*see* Chapter 10).
6. **Retinal dysplasia** is characterized by a congenital pink or white retrolental membrane in a microphthalmic eye, with a shallow anterior chamber and elongated ciliary processes. Unilateral cases are usually not associated with systemic abnormalities. Patients with bilateral involvement may



Fig. 11.73
Vesiculobullous dermatitis in incontinentia pigmenti

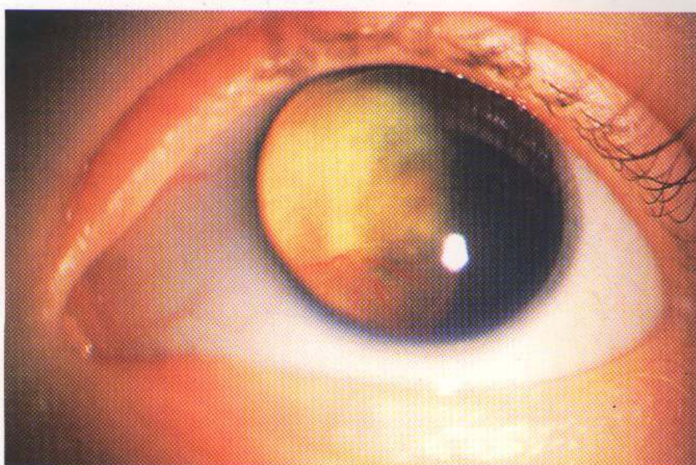


Fig. 11.74
Cicatricial retinal detachment in incontinentia pigmenti

have Norrie disease or Warburg, Patau and Edward syndromes.

7. **Incontinentia pigmenti** (Bloch–Sulzberger syndrome) is a rare X-linked dominant disorder affecting girls. It is characterized by vesiculobullous dermatitis (Fig. 11.73) on the trunk and extremities. Malformations of teeth, hair, nails, bones and central nervous system may also be present. About one-third of children develop cicatricial retinal detachment which may cause leukocoria in the first year of life (Fig. 11.74).
8. **Retinocytoma** (retinoma) is thought to be a benign variant of retinoblastoma. It is characterized by calcified mass associated with RPE alteration and chorioretinal atrophy (Fig. 11.75). The appearance is remarkably similar to that of a retinoblastoma following irradiation (*see* Fig. 11.66).
9. **Retinal astrocytoma** (*see* below).

Retinal astrocytoma

Astrocytoma of the retina or optic nerve head is a rare, benign, non-vision-threatening tumour. It may occur in

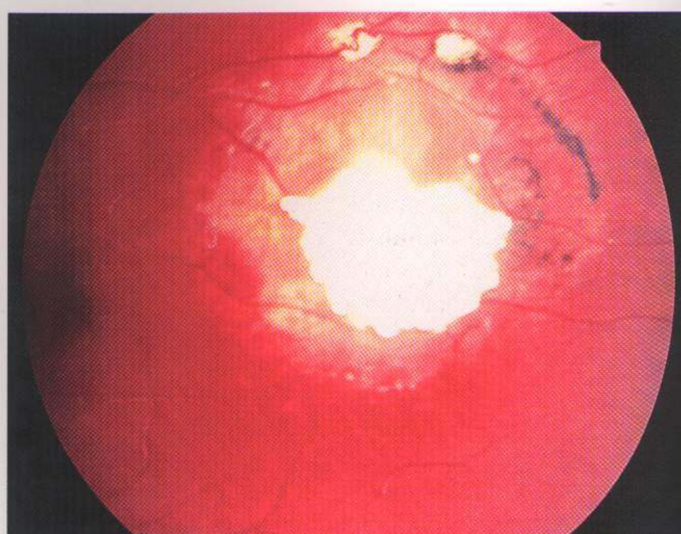


Fig. 11.75
Retinocytoma (Courtesy of K. Nischal)

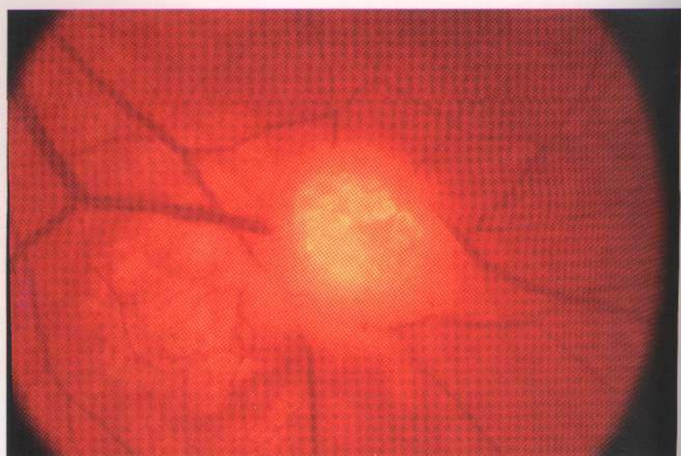


Fig. 11.76
Nodular retinal astrocytoma

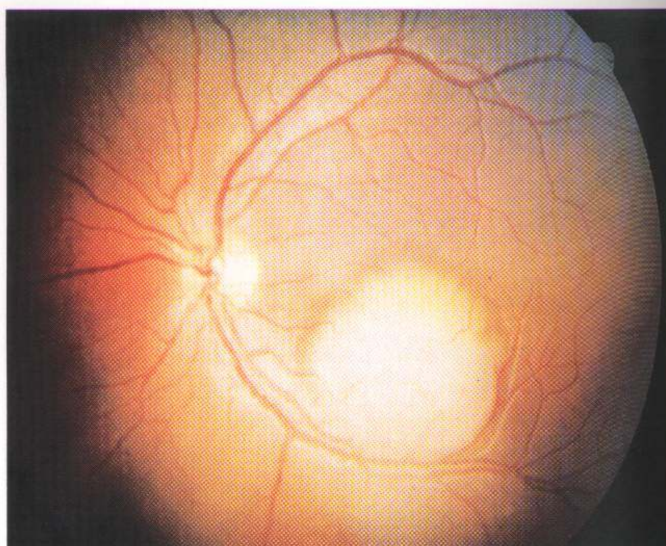


Fig. 11.77
Flat retinal astrocytoma (Courtesy of C. Barry)

isolation but is most frequently seen in patients with tuberous sclerosis (*see* Chapter 20). About 50% of patients with tuberous sclerosis have fundus astrocytomas, which may be multiple and are bilateral in about 15% of cases.

Signs

- A semi-translucent nodule (Fig. 11.76) or a white, relatively flat, well-circumscribed plaque (Fig. 11.77).
- Later, the tumour becomes more solid and white and may, on cursory examination, resemble retinoblastoma (Fig. 11.78).
- Multiple areas of calcification within a long-standing tumour may give rise to a fossilized, mulberry-like appearance (Fig. 11.79).

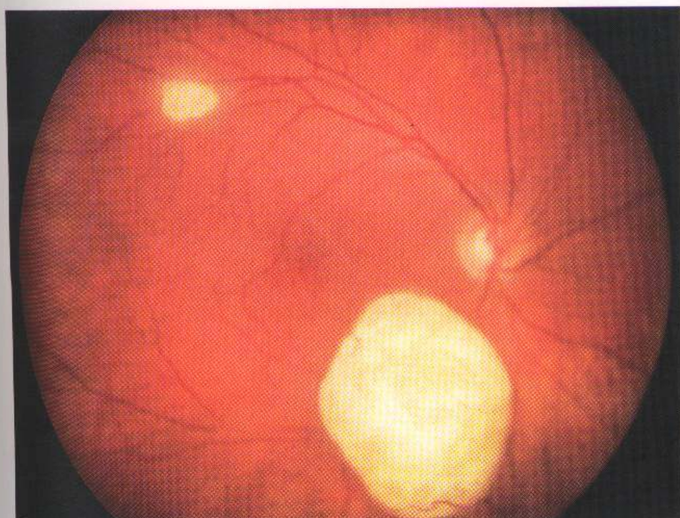


Fig. 11.78
Long-standing retinal astrocytomas

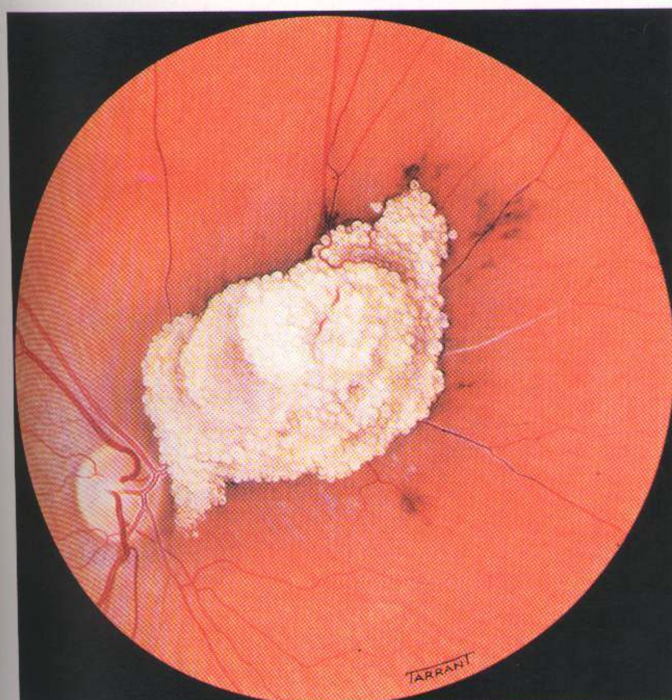


Fig. 11.79
Calcified mulberry-like retinal astrocytoma

Retinal capillary haemangioma

Capillary haemangioma of the retina or optic nerve head is a rare, sight-threatening vascular hamartoma which may occur in isolation (von Hippel disease). However about 50% of patients with solitary capillary haemangiomas and virtually all patients with multiple lesions have systemic disease. The combination of systemic and ocular lesions is referred to as the von Hippel–Lindau syndrome (V-H-L) (*see* Chapter 20). The prevalence of retinal capillary haemangiomas in patients with V-H-L is approximately 60%.

Endophytic

1. **Presentation** is in the second to third decades with unilateral or bilateral ocular involvement on screening, or with visual impairment.
2. **Signs** (in chronological order)
   - A tiny red lesion located within the capillary bed between an arteriole and a venule (Fig. 11.80).

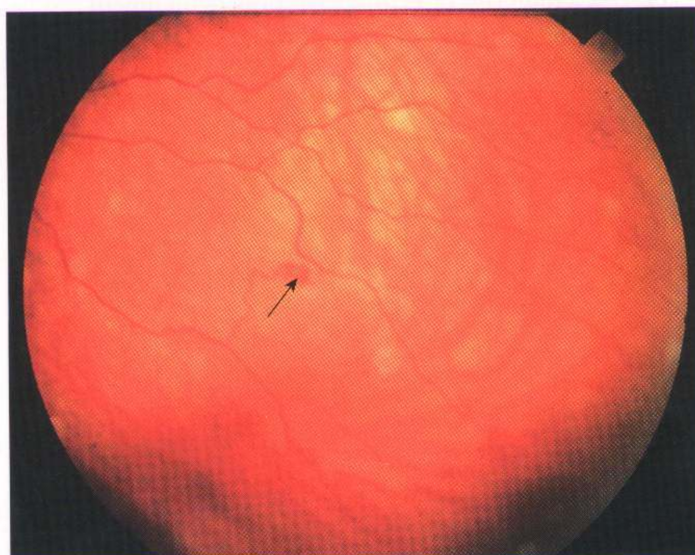


Fig. 11.80
Early retinal capillary haemangioma

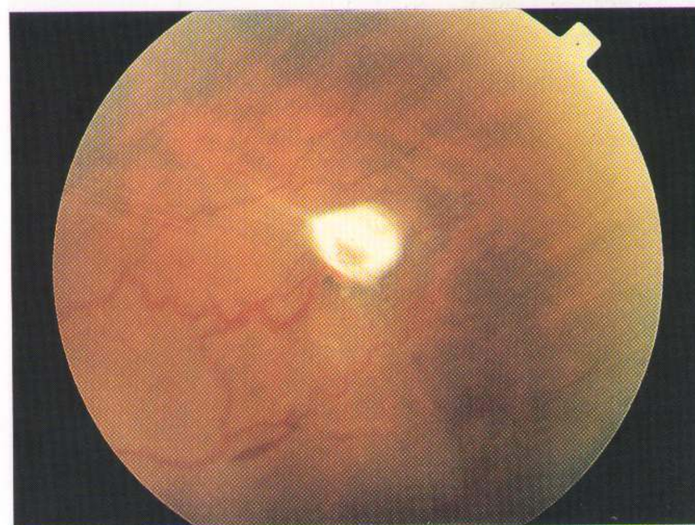


Fig. 11.81
Retinal capillary haemangioma (Courtesy of S. Milewski)

- A small, well-defined nodule (Fig. 11.81).
- A round orange-red mass associated with dilatation and tortuosity of the supplying artery and draining vein due to arteriovenous shunting so that both vessels appear similar (Fig. 11.82).

3. **FA** shows early hyperfluorescence (Fig. 11.83a) and late leakage (Fig. 11.83b).
4. **Complications** include hard exudate formation in the area surrounding the tumour and/or at the macula (*see* Fig. 11.85), macular oedema, epiretinal membrane formation, retinal detachment which may be tractional or exudative, and vitreous haemorrhage.

Other types

1. **Exophytic haemangioma** is less common, arises from the outer retina in the juxtapapillary region and presents with visual loss. It is characterized by a sessile, ill-defined lesion with dilated blood vessels, which may be associated with retinal oedema and haemorrhage (Fig. 11.84). It carries a high risk of exudative retinal detachment.
2. **Optic nerve head haemangioma** (Fig. 11.85)

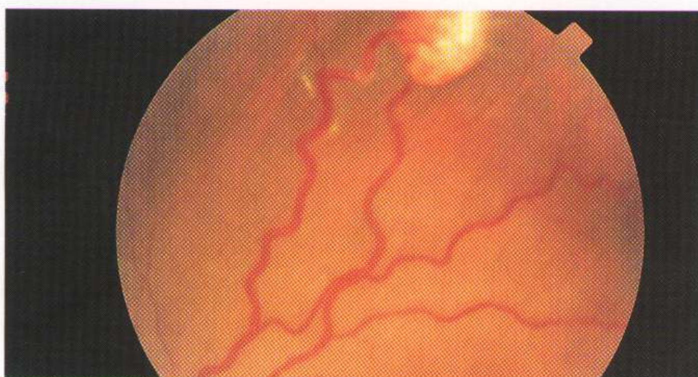


Fig. 11.82
Vascular dilatation and tortuosity associated with a retinal capillary haemangioma

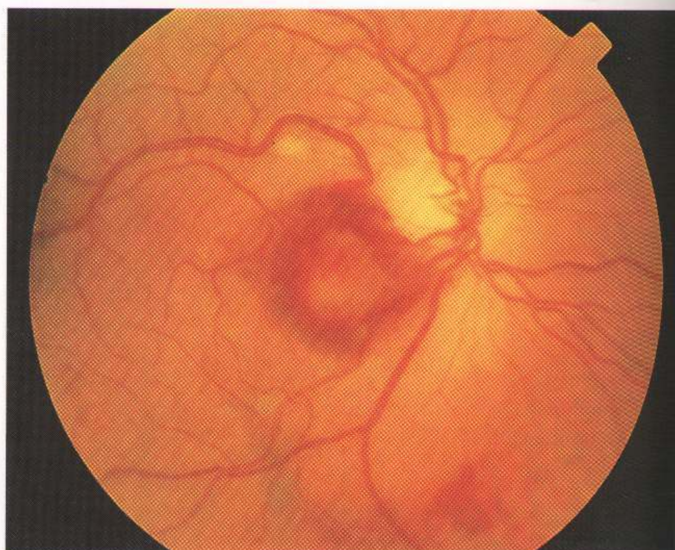
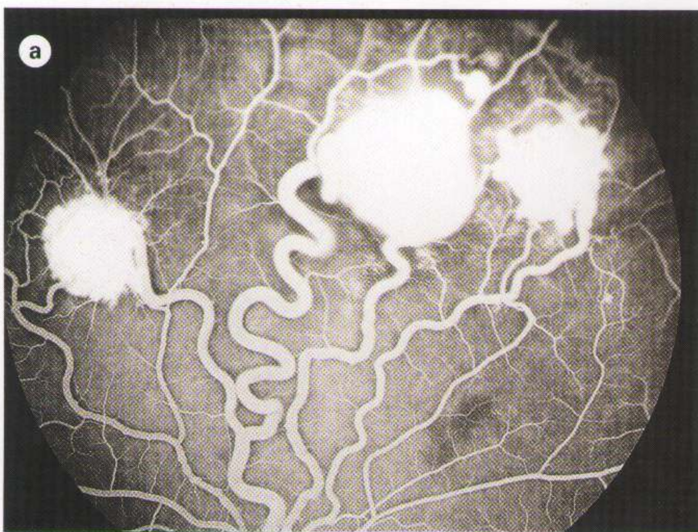


Fig. 11.84
Exophytic retinal capillary haemangioma (Courtesy of S. Milewski)

Treatment

1. **Argon laser photocoagulation** for small peripheral lesions (Fig. 11.86a). Following successful treatment the calibre of the feeding blood vessels returns to normal (Fig. 11.86b).
2. **Cryotherapy** for larger peripheral lesions or those with exudative retinal detachment. Vigorous treatment of a large lesion may cause a temporary but extensive exudative retinal detachment.
3. **Brachytherapy** for lesions one to two disc diameters in size.
4. **Vitreoretinal surgery** may be required for non-absorbing vitreous haemorrhage, epiretinal fibrosis or tractional retinal detachment. If appropriate, the tumour may be destroyed by endolaser photocoagulation.



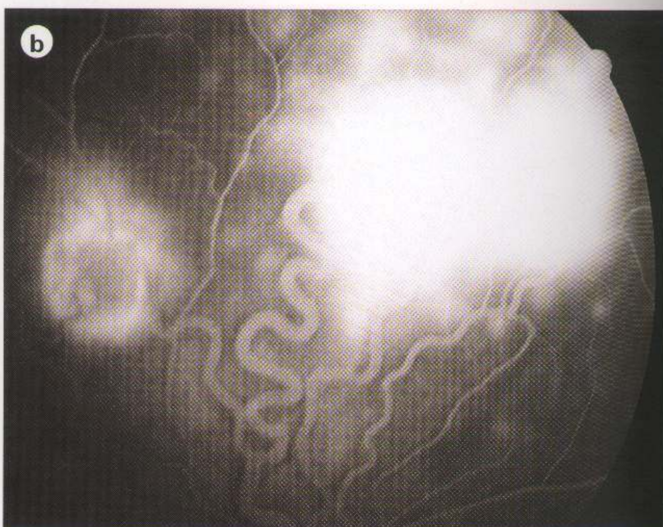


Fig. 11.83
(**a**) Early FA of multiple retinal capillary haemangiomas showing hyperfluorescence due to filling; (**b**) late phase showing leakage (Courtesy of S. Milewski)

Screening

Because it is impossible to predict which patients with retinal angiomas will also harbour systemic lesions, the ophthalmologist must refer all such patients for systemic and neurological evaluation. Relatives should also be screened because of the dominant inheritance pattern of the disease. Apart from physical examination, the following screening protocol should be regularly performed in patients with established V-H-L and relatives at risk:

1. **Annual screening**
   - Eye examination, physical examination and blood pressure measurement.
   - Renal ultrasonography from age 16 years.
   - Twenty-four hour urine collection for estimation of vanillyl mandelic acid and catecholamine levels from age 10 years to detect phaeochromocytoma.
2. **Screening every 3 years** involves abdominal and brain MRI scans from age 15 years.

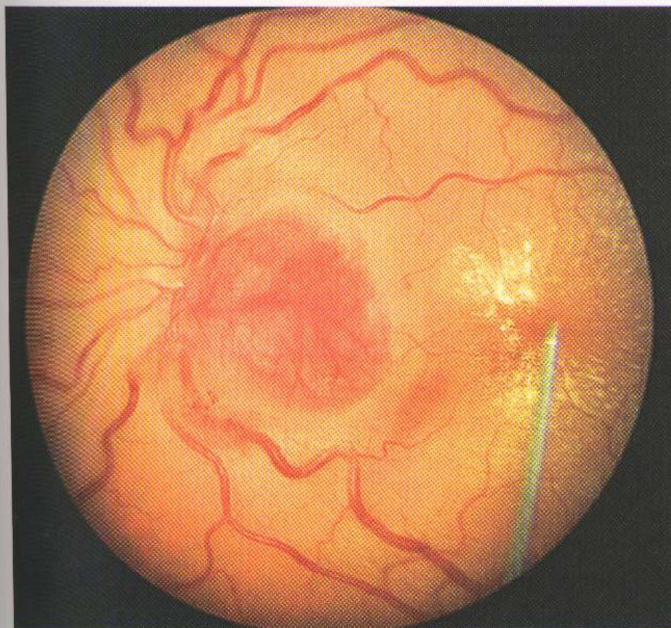


Fig. 11.85
Capillary haemangioma of the optic nerve head with macular exudates (Courtesy of K. Nischal)

Retinal cavernous haemangioma

Cavernous haemangioma of the retina or optic nerve head is a rare, congenital, unilateral, vascular hamartoma. A minority of patients have similar lesions of the skin and CNS. The combination is inherited in autosomal dominant fashion and is referred to as *neuro-oculocutaneous phacomatosis* or alternatively as *cavernoma multiplex*.

1. **Presentation** is in the second to third decades with vitreous haemorrhage, or more often as a chance finding.
2. **Signs** vary from a collection of aneurysms (Fig. 11.87) to an elaborate complex of vascular anomalies on the retina (Fig. 11.88) or optic nerve head (Fig. 11.89) which may rarely bleed (Fig. 11.90). Because of sluggish flow of blood, the red cells may sediment and separate from plasma, giving rise to 'menisci', or fluid levels within the lesion.
3. **Treatment** is generally not required although vitrectomy may be necessary in the rare event of non-absorbing vitreous haemorrhage.



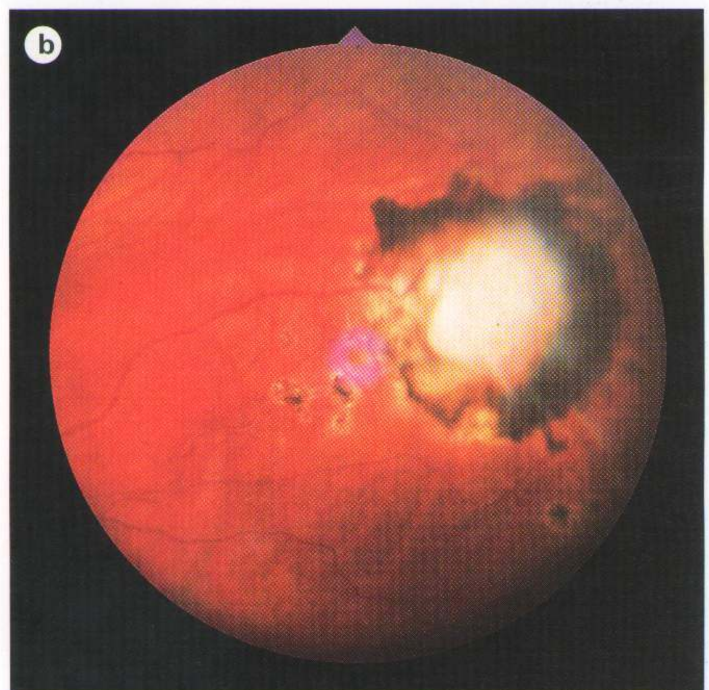


Fig. 11.86
(a) Retinal capillary haemangioma; (**b**) following laser photocoagulation



Fig. 11.87
Small retinal cavernous haemangioma (Courtesy of S. Milewski)

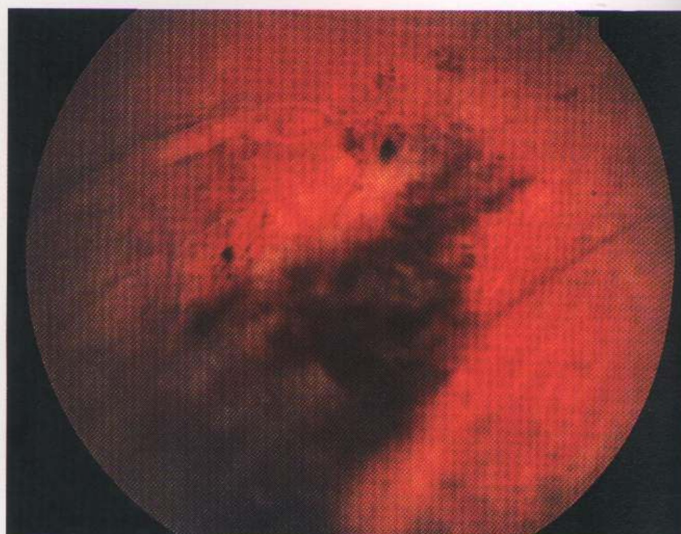


Fig. 11.90
Haemorrhage from retinal cavernous haemangioma

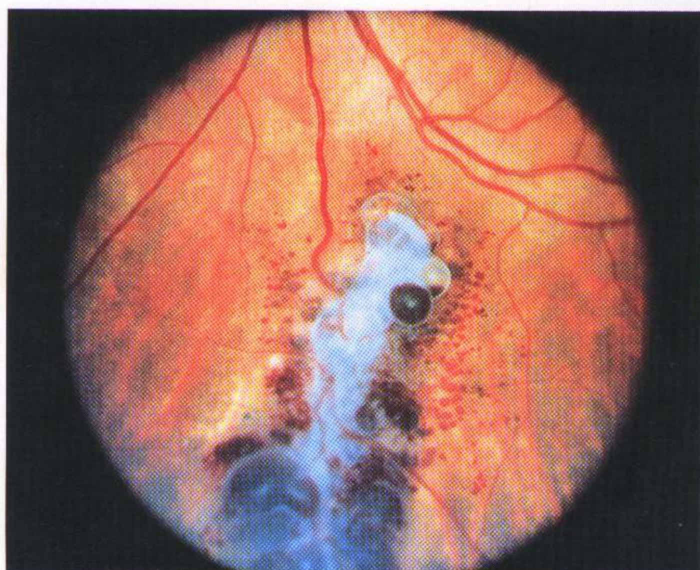


Fig. 11.88
Retinal cavernous haemangioma

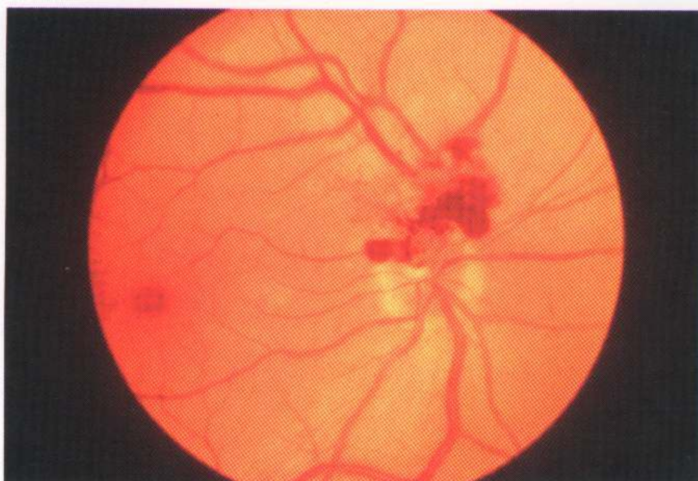


Fig. 11.89
Cavernous haemangioma of the optic nerve head (Courtesy of P. Morse)

Retinal racemose haemangioma

Racemose haemangioma of the retina and optic nerve head is a rare, usually unilateral, congenital arteriovenous malformation involving direct communication between the arteries and veins without an intervening capillary bed. Some patients have similar ipsilateral lesions involving the midbrain, basofrontal region and posterior fossa, an association which is referred to as the *Wyburn–Mason syndrome*. Brain involvement may lead to spontaneous haemorrhage or epilepsy. Occasionally, malformations may involve the maxilla, mandible and orbit. Facial skin lesions have also been reported.

1. **Presentation** may be with visual impairment or more commonly as a chance finding.
2. **Signs**. Enlarged, tortuous blood vessels which are often more numerous than in a normal fundus, with the vein and artery appearing similar (Fig. 11.91a).
3. **FA** shows absence of leakage (Fig. 11.91b–d) but very large lesions may occasionally lead to exudation and haemorrhage.
4. **Treatment** is not required.

Retinal vascular proliferative tumour

Retinal vasoproliferative tumour is a rare gliovascular lesion which occurs mostly in healthy individuals. It can be mistaken for a variety of other entities, most notably retinal angiomas, amelanotic choroidal melanomas and retinal telangiectasia.

1. **Presentation** is in the fifth to sixth decades with blurring of vision due to macular exudation.
2. **Signs**. A solitary, highly vascularized, yellow, retinal or subretinal mass with normal feeding and draining vessels (Fig. 11.92).
3. **Complications** include haemorrhage, exudation, cystoid macular oedema, epiretinal fibrosis and exudative retinal detachment.

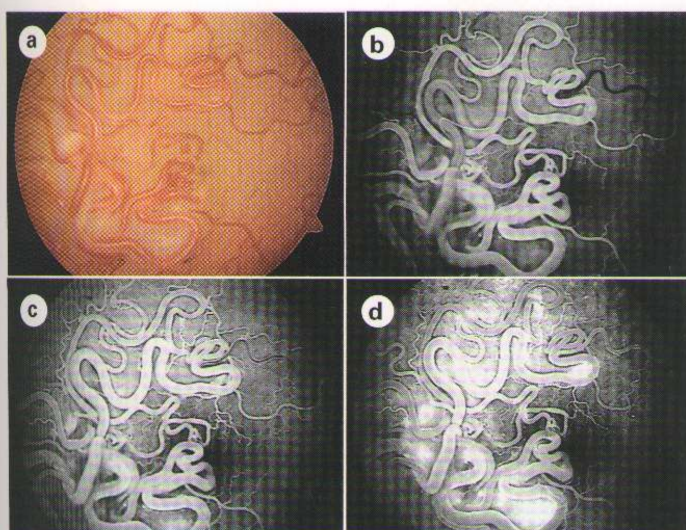


Fig. 11.91
(a) Retinal racemose haemangioma; (b–d) FA showing filling but no leakage (Courtesy of M. Karolczak-Kulesza)

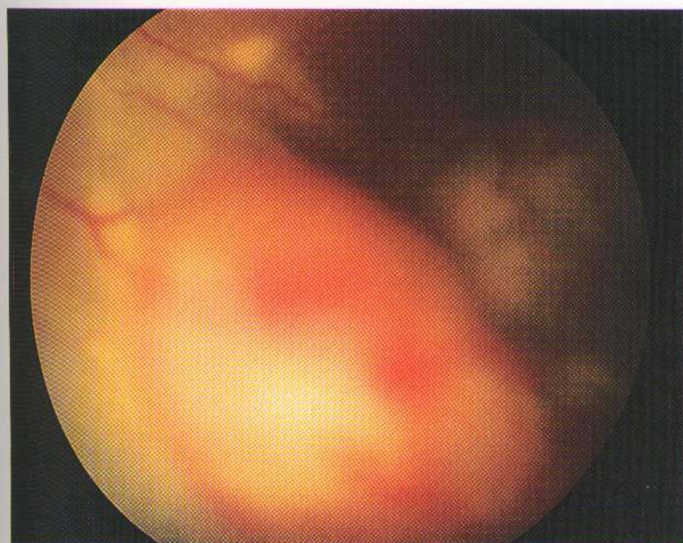


Fig. 11.92
Retinal vascular proliferative tumour (Courtesy of B. Damato)

4. **Treatment** with cryotherapy, laser photocoagulation or brachytherapy may be beneficial but the visual prognosis is guarded.

Tumours of the retinal pigment epithelium

Congenital hypertrophy of the retinal pigment epithelium

Congenital hypertrophy of the retinal pigment epithelium (CHRPE) is a common benign lesion that may be (a) *typical*, which may be solitary or grouped, or (b) *atypical*. It is important to differentiate the two types because the latter has important systemic implications.

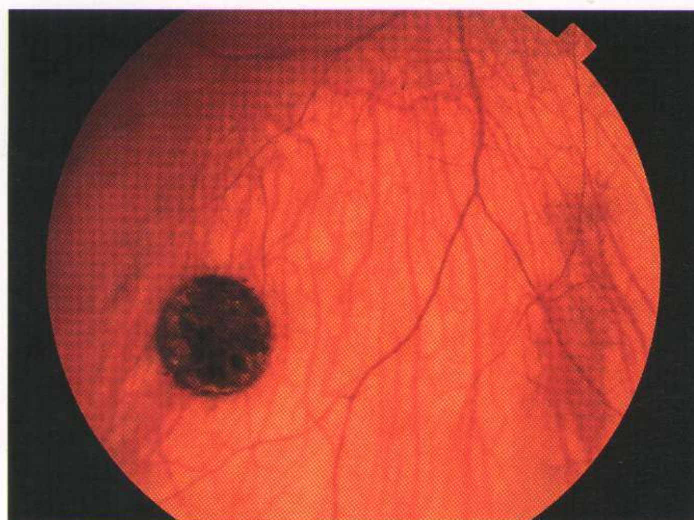


Fig. 11.93
Typical solitary congenital RPE hypertrophy with peripheral depigmentation

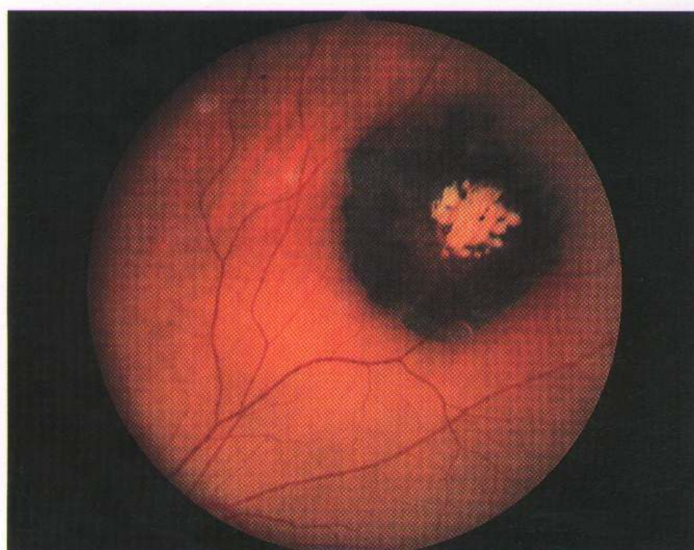


Fig. 11.94
Typical solitary congenital RPE hypertrophy with hypopigmented central lacunae

Typical CHRPE

1. **Solitary**
   - A unilateral, flat, dark-grey or black, well-demarcated, round or oval lesion one to three disc diameters in size frequently with a hypopigmented rim just within the outer margin (Fig. 11.93).
   - Depigmented lacunae which often enlarge or coalesce may be observed, particularly in older patients (Fig. 11.94).
   - Some lesions may become depigmented with only a thin rim of residual pigment remaining at the margin (Fig. 11.95).
2. **Grouped**
   - Usually unilateral, variably sized, sharply circumscribed, round, oval dark-grey or black lesions, often organized in a pattern simulating animal footprints (bear-track pigmentation) (Fig. 11.96).

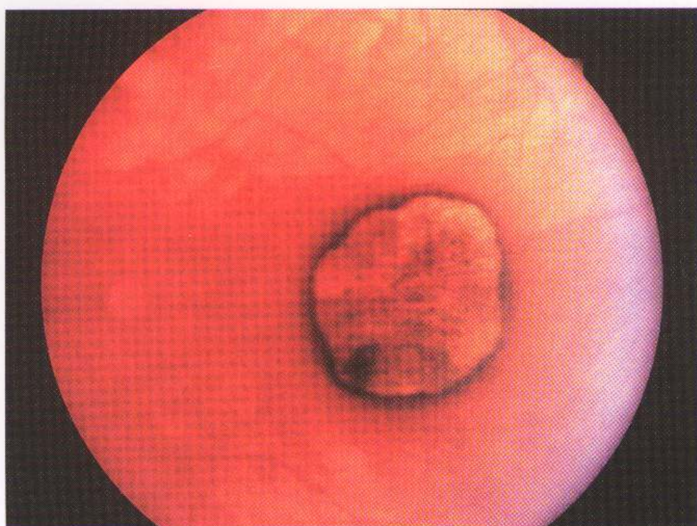


Fig. 11.95
Typical solitary congenital RPE hypertrophy which is nearly completely hypopigmented apart from a peripheral ring

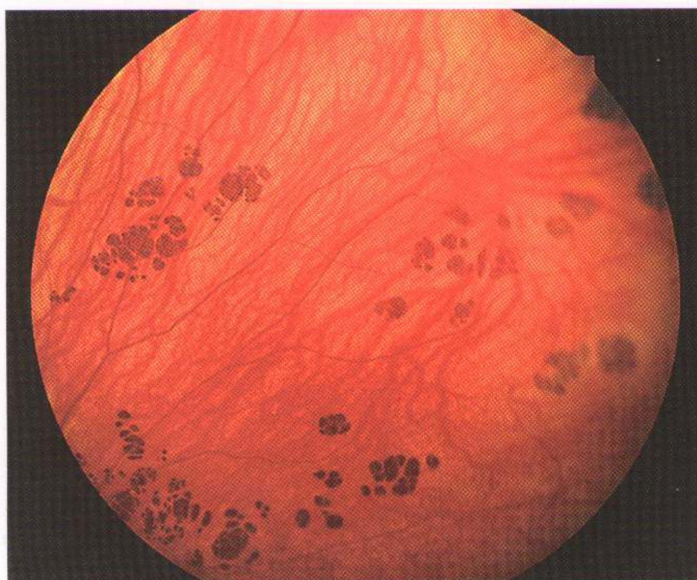


Fig. 11.96
Typical grouped congenital RPE hypertrophy

- The lesions are often confined to one sector or quadrant of the fundus, with the smaller spots usually located more centrally.

Atypical CHRPE

1. Signs

- Multiple, bilateral, widely separated, frequently oval or spindle-shaped lesions of variable size associated with hypopigmentation at one margin (Fig. 11.97).
- The lesions have a haphazard distribution and may be pigmented, depigmented or heterogenous.

2. Systemic implications

a. Familial adenomatous polyposis (FAP) is a dominantly inherited condition characterized by adenomatous polyps throughout the rectum and colon which usually start to develop in adolescence (Fig. 11.98). If untreated, virtually all patients with FAP develop carcinoma of the colorectal region by the age of 50 years. From the age of 10 years, persons at risk should undergo regular endoscopic examinations and a prophylactic total colectomy should be performed early in adult life in all affected persons. As a result of the dominant inheritance pattern, intensive survey of family members is imperative. The FAP gene has been identified on 5q21–q22. Thus, molecular genetic analysis may identify carriers of the disease in selected cases. Over 80% of patients with FAP have atypical CHRPE which is present at birth. A positive criterion for FAP is the presence of at least four lesions whatever their size, or at least two lesions one of which must be large. Such fundus lesions in a family member should therefore arouse suspicion of FAP.

b. Gardner syndrome is characterized by FAP, osteomas of the skull and mandible and cutaneous soft tissue tumours such as epidermoid cysts, lipomas and fibromas.

c. Turcot syndrome is characterized by FAP and tumours of the CNS, particularly medulloblastoma and glioma.

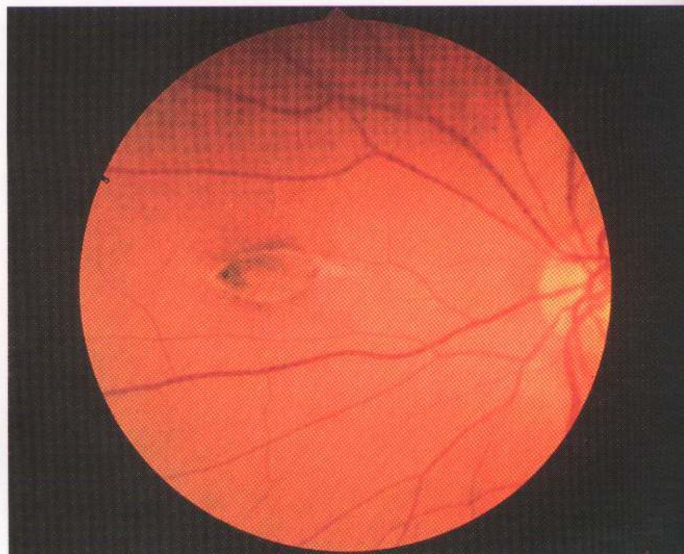


Fig. 11.97
Atypical congenital RPE hypertrophy (Courtesy of B. Jay)

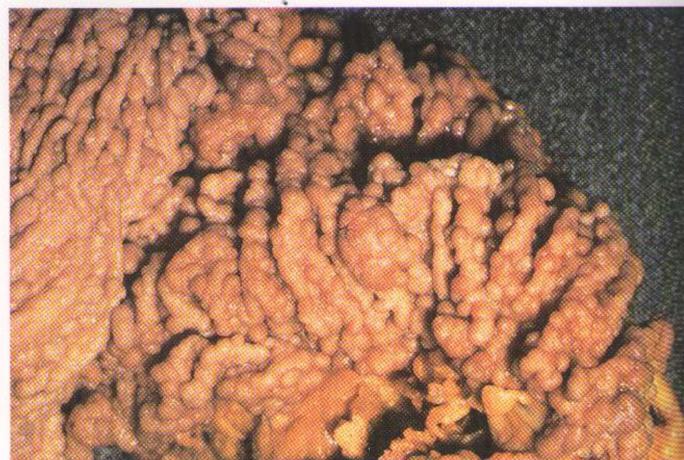


Fig. 11.98
Intestinal adenomatous polyposis

Combined hamartoma of the retinal pigment epithelium and retina

Combined hamartoma of the RPE and retina is a rare, usually unilateral malformation which may be juxtapapillary or peripheral. It predominantly affects males and is found with increased frequency in patients with neurofibromatosis-2.

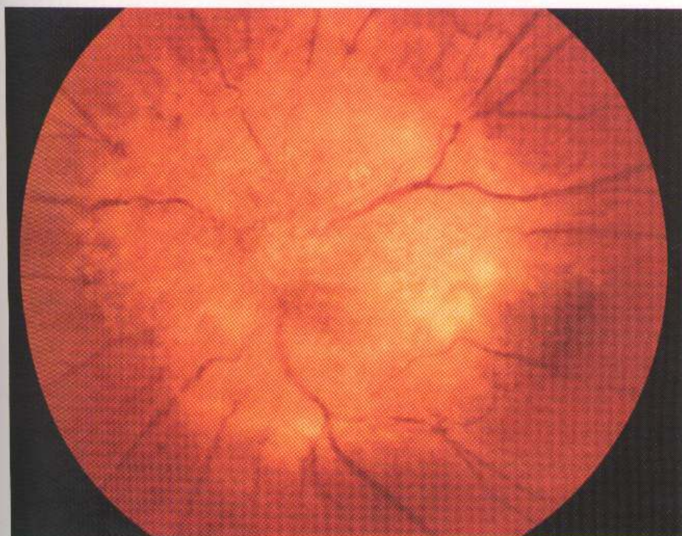


Fig. 11.99
Juxtapapillary combined hamartoma of the RPE and retina

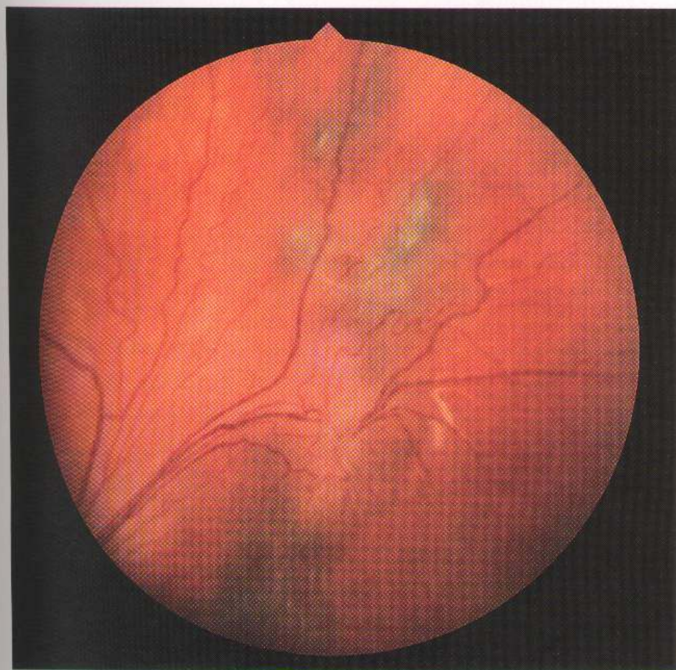


Fig. 11.100
Distortion of the retina by a combined hamartoma of the RPE and retina

1. **Juxtapapillary**
   a. ***Presentation*** is in late childhood or early adulthood with blurred vision and metamorphopsia.
   b. ***Signs***. Deep, slightly elevated, greyish-brown pigmentation associated with variable intra- and epiretinal gliosis, a fine network of dilated capillaries and vascular tortuosity (Fig. 11.99).
2. **Peripheral**
   a. ***Presentation*** is in early childhood with strabismus.
   b. ***Signs***. A linear ridge associated with stretched blood vessels.
3. **Complications** include retinal and/or optic nerve head distortion (Fig. 11.100), macular oedema, choroidal neovascularization and, rarely, retinoschisis and retinal detachment.
4. **Treatment** of epiretinal membranes by vitreoretinal surgery may be tried but the visual results are often disappointing.

Hamartoma of the retinal pigment epithelium

This is an uncommon, small, jet-black lesion involving the RPE, often at the macula, which has a tendency to spill onto the surrounding inner retinal surface (Fig. 11.101).

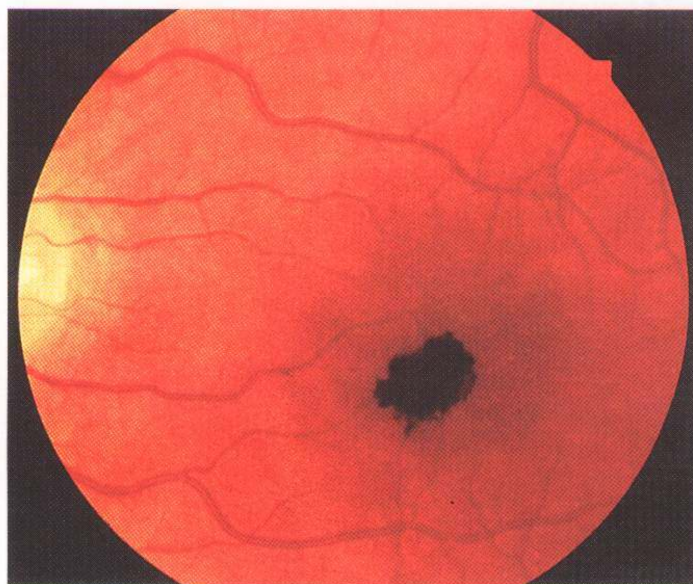


Fig. 11.101
Hamartoma of the RPE